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NONSPECIFIC TREATMENT OF PNEUMONIA IN INFANTS AND CHILDREN

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BOSTON

THE treatment of pneumonia in infants and children has become increasingly efficient within the last few years. Although we have used specific chemicals and serums for the treatment of pneumonia at the Boston Floating Hospital and still use them in selected cases, we have continued the use of nonspecific therapy in the treatment of all infants and children ill with pneumonia. This paper will concern itself with a description of these general nonspecific methods and the results exclusively achieved by them.

The seriousness of pneumonia in infancy and childhood, with all but the more recent methods of treatment, was well stated in 1916 by Morse,[1] who said: "Pneumonia is a comparatively mild disease in childhood. It is the exception for a child to die of an uncomplicated pneumonia. In infancy, however, pneumonia is a very serious and often fatal disease. The mortality in hospitals varies between 25 and 33 per cent." The following series of pneumonia patients under two years of age treated by nonspecific means confirm Morse's estimates:

Kohn and Weiner,[2] 1926–1933; 534 cases, mortality 32 per cent.

Nemir, Andrews and Vinograd,[3] 1931–1935; 526 cases, mortality 31 per cent.

McNeil, Macgregor and Alexander,[4] 1921–1928; 310 cases, mortality 44 per cent.

The efficacy of treatment that is restricted to nonspecific means as carried out in the Boston Floating Hospital from 1932 through the first four months of 1939 may be judged from Table 1. These patients came chiefly from the economically handicapped: the average family was composed of six to eight persons; the average income was under fifteen dollars a week; and the average rent for living quarters was under fifteen dollars a month. For the most part the homes were located in crowded low-rental districts of Metropolitan Boston.

The methods which we used to increase the resistance of infants and children by nonspecific means were those that conserve the energy of the patient, those that provide ample nutrition and those that seem to raise immunologic resistance to the invading organism.

TABLE 1. *Pneumonia Cases by Years.*

YEAR	INFANTS (UNDER 2 YR.)			CHILDREN (2–12 YR.)		
	NO. OF CASES	NO. OF DEATHS	PERCENTAGE MORTALITY	NO. OF CASES	NO. OF DEATHS	PERCENTAGE MORTALITY
1932	65	20	30	42	0	0
1933	36	9	25	25	2	8
1934	43	7	16	24	0	0
1935	70	7	10	45	0	0
1936	92	10	11	68	4	6
1937	73	7	10	24	0	0
1938	43	0	0	50	1	2
1939 (4 mo.)	50	2	4	26	0	0

One of the most important principles of the nonspecific therapy of pneumonia was conservation of the patient's energy. The measures employed included increasing the oxygen of the inspired air, judicious use of sedatives and efficient nursing care.

Tissue anoxia produces a sequence of events similar to functional hyperemia caused by inflammation. Moon[5] states: "Once the lack of oxygen in a large area of tissue reaches the point where capillaries and venules lose their tonus and become abnormally permeable, plasma

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escapes into the tissues and blood corpuscles are concentrated into minute vessels. This further impedes the circulation and decreases the volume flow, lowers the blood volume and increases the anoxia. With increasing anoxia the re-establishment of circulatory efficiency becomes progressively more difficult." This conception of the effect of anoxemia prompts a liberal use of oxygen for pneumonia, particularly during infancy when the pathologic effect of anoxemia may blend with that produced by the infection.

The average amount of oxygen used per patient at the Boston Floating Hospital is shown in Table 2. Commercial oxygen, which is just

TABLE 2. *Oxygen-Consumption and Transfusion Data.*

YEAR	AVERAGE AMOUNT OF OXYGEN USED PER PATIENT (ALL AGES)	PERCENTAGE TRANSFUSED (UNDER 2 YR.)	PERCENTAGE MORTALITY (UNDER 2 YR.)
	cu. ft.		
1932		30	30
1933		53	25
1934	200	32	16
1935	200	71	10
1936	500	71	11
1937	600	76	10
1938	400	70	0
1939	400	93	4

as good for these purposes as the chemically pure product, was purchased for one cent a cubic foot in tanks holding 220 cubic feet. A concentration of 40 to 60 per cent oxygen in a suitable tent may be maintained for twenty-four hours with about 300 cubic feet of oxygen. Gas under such great pressure as exists in the tank requires the use of a good reducing valve, which costs at least twenty-five dollars. A motor-driven unit required for cooling and circulating the air-oxygen mixture costs one hundred dollars and a tent enclosure an additional fifty dollars. G. W. Ettinger of the Boston Floating Hospital staff has built both these for us. In their construction he used a copper coil, a steel container and a second-hand vacuum-cleaner motor; all these materials cost only twelve dollars. For the tents he used a cellophane-like material (Transnental cloth), fifty yards (costing nineteen dollars) being sufficient for seventeen tents. The frames were made of strap iron.

In carrying out the therapy, the oxygen of the inspired air was measured and recorded at least every two hours. For this purpose a simple apparatus devised by Emerson and Company, of Cambridge, Massachusetts, was used. A sample of the air-oxygen mixture near the patient's face was drawn into a 10-cc. syringe. This mixture was introduced through a small glass tube into a testing solution made up of saturated ammonium chloride three parts and ammonia water (28 per cent) one part. Copper shavings (a scouring cloth is quite suitable) were immersed in this fluid. After two or three minutes the unabsorbed gas in the cylinder was redrawn into the syringe, all the oxygen having combined with the copper. The accuracy of the testing solution was checked with room air. Regular checking of the inspired air-oxygen mixture is essential, and if necessary the ratio of oxygen to air should be stepped up in order to maintain the desired level; a few hours of anoxemia during a critical period may prove fatal. The danger of explosions, resulting from the use of oxygen under pressure, should always be kept in mind.

A relative humidity of 40 to 50 per cent makes breathing easier and permits better drainage of secretions from the respiratory tract. The humidity within the tent should be measured once or twice a day by means of a wet-and-dry-bulb thermometer. The humidity is generally found to be within the desired range if the temperature in the tent is kept between 75 and 80°F. Under these conditions all clothing may be removed from the chest and abdomen, which permits greater freedom of movement. This also gives the physician and nurse a better opportunity of observing the respiratory movements.

Older children were allowed to assume the position of choice; infants were placed in various positions, until the most comfortable one was found. Many children and older infants assumed the knee-chest position. Small infants generally seemed more comfortable lying prone with the head lower than the chest, but some of them breathed more easily in a supine position with the shoulders elevated and the head and neck in partial extension. Removal of tenacious secretion from the upper respiratory tract by a suction machine or an aspirating bulb usually induced peaceful sleep.

Sedatives judiciously used aid in conserving the energy of a pneumonic infant or child. Morphine sulfate is our choice. The variation of effect produced from patient to patient and from dose to dose is less marked with morphine sulfate administered subcutaneously than with other drugs given by the same or other routes. A rapid, shallow type of breathing with a quick inspiratory effort immediately following expiration generally becomes deeper and more relaxed with this sedative. This makes oxygen therapy more effective. Moreover, morphine used in connection with oxygen therapy usually changes a struggling, frightened child who is not taking enough nourishment to one who is well poised, partially relaxed and eager for food.

Morphine sulfate was given according to the

body weight, 1/6 gr. for a 75-pound child, 1/12 for a 30-pound child, 1/24 for a 15-pound infant and so on. Except under unusual circumstances no more than two consecutive doses at four-hour intervals were ordered without seeing the patient. Reaction to the morphine was carefully observed, especially that due to the first dose. Idiosyncrasies usually manifested by marked excitability occurred in about 2 per cent of the patients.

All sedatives are contraindicated if there is difficult breathing caused by tenacious secretion, peripharyngeal or retropharyngeal swellings, severe tracheobronchitis or rapid accumulation of air or fluid in the pleural space, and they, of course, should not be given to moribund patients or to those who are in the excited stage preceding collapse from anoxemia. Morphine generally masks the pain due to otitis media, with the exception of those cases in which swallowing is painful because of referred pain via the glossopharyngeal nerve; consequently the complication of acute otitis media should always be looked for and treated appropriately. The responsibility for the use of sedatives for an acutely ill infant or child should rest entirely on the physician.

The standard of nursing care depends chiefly on the physician's anticipating the difficulties that may be encountered and also on the example he sets. For instance, if he removes an anoxemic patient from the tent for long periods without evident concern, the nurse is apt to do likewise. In some hospitals where medical supervision is not rigid and lay or nursing administration has taken over details of medical supervision, physicians may have difficulty in establishing a physician-nurse relation that affords the optimum conditions for proper protection of the patient. Rapid changes in nursing personnel are particularly bewildering, but good descriptive nursing notes, well supervised by reliable ward supervisors, help to overcome this difficulty. Above all, gentleness, patience and a sense of responsibility are essential qualities.

The nutrition of an infant or child with pneumonia is of great importance in treatment. Consequently the nutritional history and the physical signs pertinent to it were closely studied. Particular attention was given to the family income with the idea of determining its adequacy for all members of that family. The family's habits of purchasing, storing and preparing its food were investigated in order to find out whether the diet contained the proper proteins, minerals and vitamins. The eating habits of mother and child were scrutinized. All these matters were investigated by the staff and by the visiting nurse, who went to the home of almost every patient for this information, not only for its bearing on the present illness but also because of its value in preventing other illness which might have a nutritional background.

In planning for proper nutriment during the acute illness, the emergency of preserving life and combating the infection outweighs the needs for optimal growth and development. Proteins and fats are not easily digested; consequently readily digestible and assimilable carbohydrates were given. This prevents unnecessary depletion of protein and provides a better source of energy during the acute illness when metabolism is increased.

Fluids should be given in ample amounts. A mixture consisting of one part normal saline, two parts fruit juice and three parts 10 per cent glucose was commonly used. Since this mixture contains food it was usually not given oftener than every four hours, the total amount for twenty-four hours ranging from 500 to 700 cc. Water should be given between feedings to make up a daily fluid intake of 1000 to 1500 cc. The patients were not disturbed during the night for feeding if sleep was sound and effective and the fluid intake reasonably adequate during the day. Whey and broth were often preferred by the older children. Large amounts of glucose mixtures in concentrations above 5 per cent were avoided because they produced abdominal distention and the passage of frothy, green, acid bowel movements. The daily intake of sodium chloride was approximately 0.1 gr. per pound of body weight, but with this amount of salt in patients with a low serum protein or excessive anoxia edema occasionally resulted. As a source of vitamin A, a concentrated fish oil was given, at least 16,000 international units; this also provided an adequate amount of vitamin D. Fifty international units of vitamin B_1 for each 100 calories in the diet was given, which was double the estimated daily requirement. If there was any reason to suspect deficiencies in the other known components of the vitamin B complex these were also given. (During convalescence all patients were provided with natural foodstuffs rich in the whole vitamin B complex.) One hundred milligrams of cevitamic acid was given daily.

The use of properly matched adult blood is an accepted means of counteracting a secondary anemia, raising the level of the serum protein and supplying factors that increase immunologic resistance. Table 2 also shows that we have steadily increased the number of transfusions given infants suffering from pneumonia. This action was taken because of the poor nutritional background of most of our patients, and because of our belief that resistance to the common bacterial invaders

is enhanced by immune factors present in average adult blood. The transfusions were generally given about twelve hours after admission: reactions were rare. It was considered a violation of the general principle of the conservation of the patient's energy to remove him from the oxygen tent during a transfusion. The seriously ill patients were transfused through the ankle vein while still in their tents. In many cases a clinical response by crisis, similar to that seen after specific serum therapy, followed transfusion. It was also thought that convalescence was more prompt and recurrences less common; proof of this, however, is lacking, for no control studies have been made. During convalescence, iron was administered orally if there was secondary anemia.

Pneumonia in infants under three months of age often presents a special problem in diagnosis. The onset may be without fever but with such gastrointestinal symptoms as vomiting and diarrhea. In these patients physical signs of pulmonary infection are delayed, and the dehydration that follows loss of fluids and electrolytes commonly equals about one fifth of the normal body weight. In our experience clinical estimation of the degree of dehydration and the associated chemical disturbances is difficult and the potential danger of the infection may not be suspected. Consequently there is a tendency to delay energetic therapy. For these reasons the management of this group was somewhat different from that of the typical pneumonia patient. Weighings were made every four hours to determine the degree of dehydration and the need for fluids. Continuous use of oxygen therapy, parenteral administration of nutrition and blood transfusions were all started promptly.

SUMMARY

In this series of cases the mortality from pneumonia was greatly reduced without the aid of specific chemicals or serums. This does not imply that these specific methods are not of value, for we now use them in almost every case.

The fact is emphasized that the nonspecific form of treatment is of the utmost importance and should be given consideration in the treatment of pneumonia in infants and children.

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THE SIGNIFICANCE OF TYPE 14 PNEUMOCOCCUS INFECTION AND THE THERAPEUTIC VALUE OF SPECIFIC RABBIT SERUM FOR THIS TYPE OF PNEUMONIA IN INFANTS AND CHILDREN*

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BOSTON

SINCE the classification of the heterogeneous Group IV pneumococci into serologically distinct species (Types 4–32),[1] Type 14 has become recognized[2–5] as the pneumococcus most frequently responsible for pneumonia during infancy and the early years of childhood. The purpose of this paper is to direct attention to the frequency, age incidence and pathogenicity of the Type 14 pneumococcus as it occurs in patients under twelve years of age, and to show the results obtained at the Infants' and Children's hospitals, Boston, in the treatment of this type of pneumonia with concentrated specific rabbit serum.

DETAILS AND METHOD OF STUDY

During the last two and a half years, pneumococcus typing has been included as part of the bacteriological investigation of all patients with pneumonia admitted to the Infants' and Children's hospitals. Cases with other forms of respiratory or focal infection have been similarly studied. Only infants and children in the first twelve years of life have been included in this report.

Sputum for cultures from patients diagnosed or suspected of having pneumonia was obtained as soon as possible after entry. With a tongue depressor the patient was induced to cough or gag, and the mucoid secretions raised were caught on a sterile cotton swab. This swab was placed at once in a centrifuge tube containing suitable culture medium and the tubes were incubated at 37°C. Sterile ascitic fluid obtained by abdominal paracentesis from young children with nephrosis was found to be an efficacious culture medium for this purpose and was used almost exclusively. An optimum growth of pneumococci for typing was usually obtained within two to six hours. The Neufeld[6] method of rapid typing was employed routinely for identification of any pneumococci present in the cultures. Material from other sources, such as pus from the ears, was similarly cultured, and occasionally typings were performed directly on the throat-swab mucus or purulent body fluids. Cultures of the blood from nearly all patients with pneumonia were taken at the time of entry or immediately prior to serum therapy. Additional cultures were made if the patient failed to improve or when earlier cultures showed growth of organisms. In order to detect mixed infection with more than one type of pneumococcus, each typing was carried out through all the Neufeld pools and for each constituent type in every pool which gave a positive *Quellung*. Blood plates were streaked in order to identify and establish the significance of any other associated organisms. In each case an attempt was made to evaluate the relative importance of all organisms cultured from various sources.

Examination of the chest by x-ray photography or fluoroscopy was obtained as soon as possible after entry so as to confirm, establish or exclude the presence of pneumonia, and repeated examinations were made as deemed advisable. In practically all the patients with Type 14 pneumonia the diagnosis was confirmed by roentgenological evidence.

No attempt was made to classify separately bronchopneumonia and lobar pneumonia. From comparison with the cases of pneumonia due to pneumococcus Type 1 the pulmonary distribution seemed to be related somewhat to age, the younger patients tending to have atypical pneumonias and the older ones a more truly lobar involvement. The type of organism responsible and the age of the patient appeared to be of more fundamental as well as of more practical importance as a basis for classification and prognosis than the necessarily arbitrary distinction based on the distribution of the pulmonary lesions.

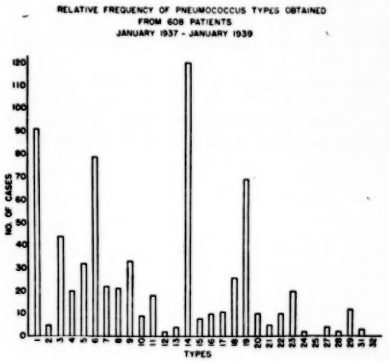

FIGURE 1.

Twelve of the 14 patients with pneumococcus Type 14 infection who died came to autopsy, and through the courtesy of Dr. Sidney Farber of the Pathology Department the postmortem findings have been incorporated with the data obtained during life.

PNEUMOCOCCUS TYPE 14 INFECTION

From January, 1937, to January, 1939, pneumococci were isolated from 608 patients with various forms of infection (Fig. 1), including approximately 400 with pneumonia. Pneumococcus Type 14, obtained from 120 or 20 per cent of all

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the cases and from 104 or 25 per cent of those with pneumonia, was the most frequent single type encountered and the dominant pneumococcal agent of pneumonia. The conditions with which the Type 14 pneumococcus was found to be associated are presented in Table 1, and the sources from which this organism was obtained are noted in Table 2.

Pneumococcus Type 14 occurred predominantly in patients with pneumonia and was invariably associated with some form of respiratory infection. Of the 16 patients in the present series the hospital. Four other infants from whom this organism was obtained in throat cultures had bronchitis and peribronchitis with associated upper respiratory infections, but without sufficient clinical or roentgenological evidence to establish the presence of a definite pneumonic process. One of these patients was ill simultaneously with Sonné dysentery. Three infants and a three-year-old child had purulent pneumococcus Type 14 otitis media with associated upper respiratory infection. In addition the Type 14 pneumococcus was obtained in throat cultures from 3 young children with upper-respiratory infections who were siblings of patients in the hospital with Type 14 pneumonia.

TABLE 1. *Conditions Associated with Pneumococcus Type 14.*

DISEASE	TOTAL NO. OF CASES	NO. OF DEATHS	AUTOPSIES	INFANTS (UNDER 2 YR.) NO. OF CASES	INFANTS (UNDER 2 YR.) NO. OF DEATHS	CHILDREN (2–12 YR.) NO. OF CASES	CHILDREN (2–12 YR.) NO. OF DEATHS
Pneumonia	104	10	9	63	8	41	2
Meningitis	4	4	3	4	4	0	0
Miliary tuberculosis	1	0*	0	1	0	0	0
Bronchitis bordering on interstitial bronchopneumonia	4	0	0	4	0	0	0
Otitis media with associated upper respiratory infection	4	0	0	3	0	1	0
Siblings of patients with Type 14 pneumonia, all with upper respiratory infection	3	0	0	0	0	3	0
Totals	120	14	12	75	12	45	2

*Patient died two weeks after discharge from the hospital.

TABLE 2. *Sources of Pneumococcus Type 14.*

WHEN OBTAINED	SOURCE	IN 104 CASES OF PNEUMONIA: NO. OF CASES	IN 104 CASES OF PNEUMONIA: NO. OF POSITIVE SPECIMENS	IN 16 CASES WITHOUT DEFINITE PNEUMONIA: NO. OF CASES	IN 16 CASES WITHOUT DEFINITE PNEUMONIA: NO. OF POSITIVE SPECIMENS
	Throat (sputum)	97	103	10	10
	Blood	8 (of 86 cases)	14	4	4
	Chest fluid	4	11	0	0
During life	Ears	19	28	5	7
	Mastoid	1	1	0	0
	Spinal fluid	0	0	4	4
	Septic joint	1	1	0	0
	Heart's blood	5 (of 7 cases)	5	3	3
	Lung	3	3	1	1
Postmortem	Pleura	4	4	0	0
(9 cases	Pericardium	3	3	0	0
pneumonia,	Mediastinum	1	1	0	0
3 cases	Ears	5	8	1	2
meningitis)	Brain	2	2	0	0
	Meninges	1	1	2	2
	Spinal fluid	0	0	2	2
Single source during life		76		12	
Multiple sources during life		20		1	
Only at autopsy		3			
During life and at autopsy		5		3	

considered not to have definite pneumonia, 4 were infants with meningitis secondary to infection of the upper respiratory passages. All the patients with meningitis also had bacteremia; none received specific serum therapy, and all died. Pneumococcus Type 14 was isolated from the throat of an infant with miliary tuberculosis who died at home two weeks after discharge from

As noted in other clinics,[4, 5] the Type 14 pneumococcus showed an extraordinarily selective distribution and pathogenicity among infants and young children of pre-school age, yielding its dominance among older children to the Type 1 pneumococcus. This is strikingly illustrated by comparing the age incidence of infection with these two types (Fig. 2). Among the patients from whom the Type 14 pneumococcus was isolated the age incidence was similar in the serum-treated and non-serum-treated groups of pneumonia patients as well as in the small group of patients without pneumonia (Fig. 3). Eighty per cent of all the patients and 79 per cent of the pneumonia patients from whom this organism was obtained were in the first three years of life. With one exception fatalities occurred exclusively in this age period.

In adults the Type 14 pneumococcus has been uncommon as the cause of pneumonia, accounting for only 3 per cent of the cases from which pneumococci have been isolated.[4, 7, 8] The frequency of its occurrence in the nasopharyngeal flora of healthy adults has not been clearly established. Among infants and children the Type 14 pneumococcus apparently occurs infrequently in the absence of pneumonia. Nemir and her asso-

ciates[5] at Bellevue Hospital studied bacteriologically 425 patients without pneumonia and found this organism in only 4.7 per cent of their cases. Long et al.[9] cultured the nasopharyngeal flora of all patients admitted to the Infants' Hospital, Bos-

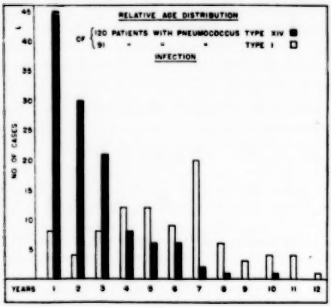
RELATIVE AGE DISTRIBUTION
OF 120 PATIENTS WITH PNEUMOCOCCUS TYPE XIV
91 " " " TYPE I
INFECTION
NO. OF CASES
YEARS 1 2 3 4 5 6 7 8 9 10 11 12

FIGURE 2.

ton, during the winter of 1937-1938. They found that Type 14 pneumococci occurred very infrequently in patients with conditions other than pneumonia and never encountered this organism caring for infants with pneumococcus Type 14 pneumonia, contracted the disease and succumbed. In 3 additional patients from whom pneumococcus Type 14 was cultured there was evidence that infection with this organism might have been acquired in the hospital. Recent epidemiological studies of the parents and siblings of patients admitted to the hospital for pneumococcus Type 14 infection indicate that family epidemics similar to those reported[10] for other types of pneumococci are not uncommon.

PNEUMOCOCCUS TYPE 14 PNEUMONIA

The factors which appeared to predispose to pneumonia in the 104 patients from whom the Type 14 pneumococcus was obtained are listed in Table 3. Acute upper-respiratory infections including colds, grippe and bronchitis, often with associated otitis media, preceded the onset of pneumonia in 66 per cent of the patients. In only 7 per cent was pneumonia secondary to a specific contagious illness or operative procedure. In an additional 13 per cent there existed an associated disease not directly related to the development of pneumonia.

The symptoms which characterized the onset of pneumonia in these cases were somewhat dependent on the age of the patient. In the infants and

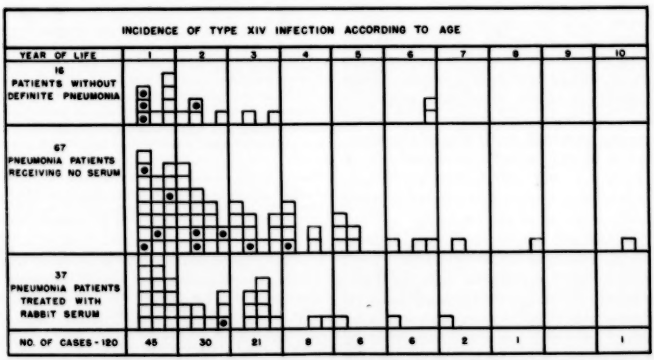
INCIDENCE OF TYPE XIV INFECTION ACCORDING TO AGE
YEAR OF LIFE 1 2 3 4 5 6 7 8 9 10
16 PATIENTS WITHOUT DEFINITE PNEUMONIA
67 PNEUMONIA PATIENTS RECEIVING NO SERUM
37 PNEUMONIA PATIENTS TREATED WITH RABBIT SERUM
NO. OF CASES - 120 45 30 21 9 6 6 2 1 1

FIGURE 3.

Each square represents a case, and each dotted square a fatality.

in a patient without some form of respiratory infection.

The communicability of infection with the Type 14 pneumococcus has been manifested by the development of acute pneumonia apparently due to this organism in 5 patients hospitalized for other conditions and in a student nurse who, while younger children, among whom preceding respiratory infection had occurred most frequently, increase of temperature, the development of grunting or rapid respirations, refusal of feedings, irritability and the appearance of a greater degree of prostration were the usual manifestations of incipient pneumonia. Of the patients with preced-

ing upper respiratory infection, evidences of pneumonia developed suddenly in 35 and gradually in 34. Of those without antecedent respiratory infection the onset was sudden in 28 and gradual in 7. Vomiting was associated with the onset or the early stages of pneumonia in 43 of the patients and convulsions in 13. Chills were noted in 9 patients, of whom only 2 were infants. Four children complained early of pleural pain. In infants there occasionally was evidence of abdominal or pleural pain which could not be separately distinguished. Meningismus was noted in 16 patients. Delirium was infrequent, but a majority of the patients appeared prostrated or toxic at the time of admission to the hospital.

TABLE 3. *Significant Predisposing Factors in 104 Patients with Pneumonia.*

PREDISPOSING FACTORS	NO. OF CASES	NO. OF RECOVERED CASES	DEATHS	POST-MORTEM EXAMINATIONS
Antecedent acute upper respiratory infection	69	61	8	7
Primary conditions to which pneumonia was secondary:				
Other infections				
Measles	2	1	1	1
Pertussis and mumps	1	1	0	0
Operative procedures				
Mastoidectomy	1	0	1	1
Appendectomy and peritonitis	1	1	0	0
Bronchoscopy*	1	0	1	1
T. and A. (with abscess)	1	1	0	0
Pre-existing or associated conditions not directly related to the development of pneumonia:				
Bronchial asthma	1	1	0	0
Mild scurvy	1	1	0	0
Celiac syndrome*	1	0	1	1
Congenital heart disease	1	0	1	0
Adrenal insufficiency	1	1	0	0
Chronic osteomyelitis of toe	1	1	0	0
Eczema	1	1	0	0
Cervical adenitis	3	3	0	0
Dysentery (*B. paratyphosus* B)	1	1	0	0
Pyelonephritis	2	2	0	0

*Type 14 was not confirmed at autopsy as the cause of pneumonia in the patient who died following bronchoscopy and the one with celiac syndrome.

Cases of pneumonia due to the Type 14 pneumococcus were clinically indistinguishable from those in which other organisms were etiologic. Although severely ill infants with pneumonia were found to harbor the Type 14 pneumococcus more frequently than any other pneumococcus type, the etiologic diagnosis could not be presumed without bacteriological evidence.

The Type 14 pneumococcus when found in infants and children with pneumonia usually appeared to be causative. Andrews[11] found it to be one of several types of pneumococcus which, in a similar age group, appeared to be causative in all patients with lobar pneumonia from whom they were recovered. In 62 per cent of the 104 patients with pneumonia in the present series it was the only organism of importance isolated. Among the 40 patients with associated pathogenic organisms (Table 4), pneumococcus Type 14 was apparently causative in 20 cases and a participating invader in 3 others. In 12 patients the relative etiologic importance of the organisms present could not be established, and in only 5 cases did associated organisms appear to be of greater significance. In evaluating the etiologic importance of the several organisms isolated from an individual patient, the relative significance of their respective sources and the clinical response to the administration of specific antiserum were the chief criteria used.

Of the 20 cases with mixed infection in which the Type 14 pneumococcus appeared to be causative, 13 yielded this organism from multiple sources, including cultures of the blood, lungs and purulent exudates. In 3 patients

TABLE 4. *Relation of Other Organisms to Pneumococcus Type 14 in 40 Patients with Pneumonia.*

OTHER ORGANISMS	NO. OF CASES*	PNEUMOCOCCUS TYPE 14 PREDOMINANT	OTHER ORGANISM PREDOMINANT	PNEUMOCOCCUS TYPE 14 AND OTHER ORGANISM CAUSATIVE	DOUBTFUL WHICH ORGANISM CAUSATIVE
Pneumococcus:					
Type 1	1	0	0	1	0
Type 4	1	0	0	1	0
Type 5	1	0	1	0	0
Type 6	5	3	0	0	2
Type 7	1	0	0	0	1
Type 15	1	0	0	1	0
Type 19	3	1	0	0	2
Type 20	1	1	0	0	0
Types 18, 19	1	0	0	0	1
Hemolytic streptococcus	9	5	2	0	2
Hemophilus influenzae	8	6	1	0	1
Staphylococcus aureus	18	12	2	0	4
Bacillus paratyphosus B	1	0	0	0	1

PROBABLY CAUSATIVE ORGANISM	NO. OF CASES
Pneumococcus Type 14	20
Other organism	5
Pneumococcus Type 14 and other organisms	3
Doubtful which organism	12
Total	40

*The sums of the cases numbered in the columns are in excess of the correct totals for each etiologic category, as 16 of the patients with mixed infections had more than one other organism associated with pneumococcus Type 14.

the Type 14 pneumococcus was obtained from a more significant source than that of the associated organism, and in the 4 other patients the prompt response to specific antiserum was the basis for considering the Type 14 pneumococcus to be etiologic.

In 3 cases pneumococcus Type 14 and the associated organisms appeared to be about equally pathogenic. In 1 of these, which received serum and is considered later in greater detail, pneumococci Types 1 and 14 were both obtained from cultures of sputum and empyema fluid. In another child who appeared desperately ill, pneumococci Types 4 and 14 were obtained simultaneously from repeated sputum cultures. After forty-eight hours of treatment with sulfapyridine and because no evident improvement had occurred, 33,000 units of Type 14 antiserum were administered intravenously. The patient showed improvement in response to this treatment but remained febrile and incompletely cured for several days. As the patient's serum showed strong agglutinins for the Type 14 pneu-

mococcus but none for the Type 4 pneumococcus following serum therapy, the evidence of persisting infection was attributed to the latter organism. In the third of these patients, a child with lung abscess and pneumonia, pneumococci Types 14 and 15 were repeatedly obtained in about equal numbers from the purulent material expectorated.

In 12 patients with pneumonia there was insufficient evidence to establish the etiologic predominance of either pneumococcus Type 14 or the associated pathogens. Both organisms were isolated simultaneously from the sputum in 6 cases and from the ears in 3. In 1 patient pneumococcus Type 14 was obtained from the sputum and *Bacillus paratyphosus* B from blood and stool cultures. Two patients with pneumococcus Type 14 in the sputum yielded *Staphylococcus aureus* in single isolated blood cultures. As preceding and subsequent blood cultures were negative in 1 of these patients and the pneumonia terminated favorably by crisis in both, the presence of *Staph. aureus* was of doubtful significance.

In only 5 cases did the associated organisms appear to be of greater significance than pneumococcus Type 14. In a child whose initial sputum culture yielded pneumococcus Type 14, ample treatment with Type 14 antiserum failed to cause improvement and pneumococcus Type 5 was subsequently isolated from the sputum and the ear. Regardless of whether or not both organisms involved the lungs, pneumococcus Type 5 apparently accounted for the therapeutic failure of Type 14 antiserum and was therefore assumed to be the dominant pathogen. In an infant who succumbed to pneumonia following bronchoscopy, pneumococcus Type 14 was isolated from the throat during life and from the ears at autopsy. *Staph. aureus* obtained from the lungs was regarded as of greater importance, although it may have been present as a secondary or terminal invader. In 2 patients hemolytic streptococci appeared to be of greater significance. In 1 of these who survived, pneumococcus Type 14 was isolated from an ear and a hemolytic streptococcus from the blood stream. In the other case pneumococcus Type 14 was cultured from the throat on the day before death, but at postmortem a hemolytic streptococcus was found in the heart's blood and *Staph. aureus* in the lung. In another patient, pneumococcus Type 14 was isolated twice from the throat and once from an ear in association with *Hemophilus influenzae*, which was grown on two occasions from the blood stream. While this probably represented actual mixed infection, the influenza bacillus was assumed to be predominant.

The severity and long duration of illness in infants and young children with Type 14 pneumonia together with the high fatality rate in infants, which during the first year of these observations approximated 20 per cent, seemed ample indication for more energetic and specific therapy. Detailed consideration of the duration of illness, the incidence of bacteremia and complications, and the fatalities which occurred among these cases will be reserved for comparison until the results of serum therapy have been evaluated.

Patients Treated with Serum

Three patients received experimental unconcentrated antipneumococcus Type 14 rabbit serum early in 1937. Of these, 1 infant responded by crisis, 1 child of two and a half was unimproved and recovered ultimately by lysis and 1 infant, treated on the fifteenth and sixteenth days of illness in the presence of bacteremia and empyema, continued an uninterrupted decline to a fatal termination one week later. As the details of administration and the antibody content of the serum used in these 3 cases is not known, they will not be included in the subsequent evaluation of serum therapy.

In March, 1938, potent concentrated antipneumococcus Type 14 rabbit serum became available and was subsequently administered to 34 of 46 consecutive patients with pneumonia from whom the Type 14 pneumococcus had been isolated. Among the 34 patients who received concentrated serum, 22 were infants under two years of age and 29 were less than three. Serum therapy was withheld for various reasons from the 12 patients who were not treated during this period, but in no sense do they comprise a control group. Seven of these 12 patients were children over two years of age; 8 entered late in the course of their disease or were recovering at the time serum administration was contemplated; 1 child had mixed infection with pneumococcus Type 15 and an associated lung abscess, following tonsillectomy; 2 patients were treated with sulfapyridine; and 1 mildly ill child was asthmatic. None of these 12 patients died, and none developed purulent complications subsequent to hospitalization.

Patients with pneumonia of less than four days' duration were deemed most suitable for serum therapy, but because of the recognized hazards of Type 14 pneumonia, treatment was not withheld from seriously ill infants and young children who entered later in the course of their disease. Only 4 infants received concentrated serum after pneumonia had been present for longer than five days (Table 5).

TABLE 5. *Duration of Acute Febrile Illness at the Time of the First Injection of Concentrated Antipneumococcus Type 14 Rabbit Serum.*

Duration	No. of Cases	No. of Improved Cases	No. of Unimproved Cases
0–1 day	4	3	1
1–2 days	9	9	0
2–3 days	9	9	0
3–4 days	4	4	0
4–5 days	4	3	1
Over 5 days	4	3	1
Totals	34	31	3

Before treatment with specific antipneumococcus serum, precautions were taken in each case to determine the presence or absence of sensitivity. A careful inquiry was made into the patient's history for manifestations of allergy, and the usual intradermal and ophthalmic tests were car-

ried out with a 1:10 dilution of rabbit serum. During the tests and administration of serum, epinephrine solution was always immediately available. No positive reactions to these tests were encountered.

In every patient receiving serum, treatment was carried out by the intravenous route. Only 1 infant was given a small additional injection intramuscularly. When the antecubital veins were inaccessible, 24-gauge needles were used and the serum was injected into venules of the extremities or scalp. With the patient held by an assisting nurse, the technical difficulties of administration never proved insurmountable.

According to the schedule of treatment gradually formulated, an initial small injection of 0.5 to 1.0 cc. of serum diluted 1:5 or 1:10 with physiologic saline was followed after intervals of two hours by larger amounts (4.5 to 10.0 cc.) of serum similarly diluted, provided no reactions had supervened. With concentrated serum of high potency, it was usually possible to administer an effective therapeutic dose in two injections. When a delayed reaction occurred, subsequent injections were deferred until all untoward manifestations had subsided. Antipyretic drugs were omitted during serum administration in order to avoid confusion of therapeutic effects.

Reactions to serum occurred in 13 of the 34 patients treated. In 6 of these cases the reactions followed administration of one of the first lots of serum used. In 4 patients the reactions occurred during or relatively soon after serum injection. Three of these, characterized by nausea and vomiting, abdominal pain or transient wheezing, were brief and relatively mild. The single severe, immediate reaction, manifested during the course of an injection by collapse and stridor, was promptly relieved by the administration of epinephrine. Nine patients had chills occurring from a half to one and a half hours after a serum injection, and accompanied in 5 of the cases by temperature elevations above 106°F. In only 1 of these patients, however, was the reaction alarming. Factors which appeared to predispose to these delayed reactions were an existing hyperpyrexia at the time of the serum injection, previous spontaneous chills or convulsions, the rapid administration of serum and the use of a lot of serum known to have produced chills previously.

Five patients showed some manifestation of serum sickness. In 3 this was represented merely by a transient rash or elevation of temperature. Two patients developed the classic picture of serum disease with associated fever and discomfort lasting for several days.

Results of Treatment with Concentrated Antipneumococcus Type 14 Rabbit Serum

The usual response to treatment with concentrated antipneumococcus Type 14 rabbit serum was prompt and gratifying, as shown in the representative individual case charts (Fig. 4). The

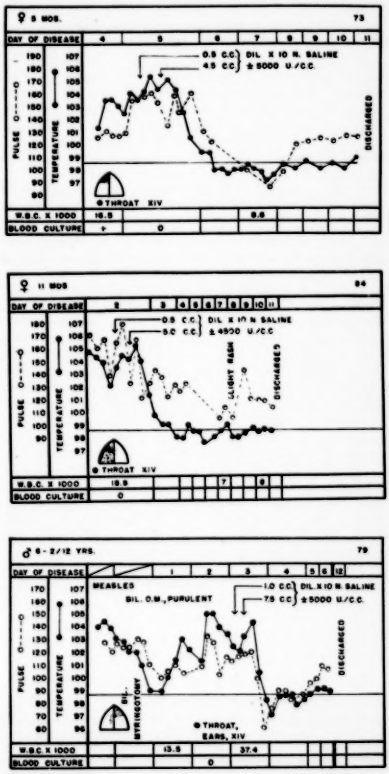

FIGURE 4.

improvement was characterized by a decline of temperature, which was frequently dramatic, accompanied or followed shortly by a fall in the pulse and respiratory rates. Subjectively and objectively the patient's general condition gave less tangible but no less striking evidences of benefit.

Thirty-one of the 34 patients who received concentrated antipneumococcus Type 14 rabbit serum

appeared to be improved by this form of therapy (Table 6). Twenty-four (71 per cent) of the

TABLE 6. *Results of Serum Administration.**

No. of Cases	Mode of Response	No. of Injections	Average Dose	Approximate Amount of Antibody
			cc.	*units*
2	Crisis	1	1.5	2,000
24	Crisis (22), lysis (2)	2	7.7	32,000
5	Crisis (2), lysis (3)	3 or more	17.0	68,000
		Averages	8.9	36,000

*Excluded are 3 patients who were unimproved by concentrated serum.

patients responded by prompt crisis within six to sixteen hours following the first injection of serum, and in a like number of cases two injections sufficed for administration of an effective therapeutic dose which averaged 7.6 cc. in volume and 32,000 units in antibody content. For the 31 cases which were benefited, 9 cc. of serum or 36,000 units of antibody was the average dose employed.

The remaining 3 cases in which concentrated antipneumococcus Type 14 rabbit serum was administered without apparent benefit are summarized below. The failure of serum therapy was attributable in Cases 1 and 2 to the presence of infection with other types of pneumococci, and in Case 3 to the presence of a purulent focus of infection (empyema) at the time treatment was started late in the course of the disease.

CASE 1. A girl of 2 5/12 years was admitted on the day of onset with pneumonia in the right upper lobe. The sputum culture yielded Type 14 pneumococcus. Blood cultures on the 2nd and 4th days of illness were sterile. Concentrated antipneumococcus Type 14 serum was given on the 2nd, 3rd and 4th days of illness (total 30 cc., 135,000 units), without improvement. On the 9th day pus from an ear and retyping of the sputum yielded Type 5 pneumococcus. The patient recovered by lysis after an acute febrile illness of 2 weeks' duration and was discharged on the 27th day.

CASE 2. A boy of 2 9/12 years was admitted on the 3rd day of illness with pneumonia in the left lower lobe. Type 1 pneumococcus was isolated from the sputum. Blood cultures on the 2nd, 6th and 13th days of illness were sterile. Concentrated antipneumococcus Type 1 serum was given on the 3rd and 4th days of illness (total 20 cc., 60,000 units), with only temporary improvement. Retyping of the sputum on the 4th day showed a few Type 1 and many Type 14 pneumococci. One cc. of antipneumococcus Type 14 serum was given on the 4th day, but as the patient was found to have developed empyema serum treatment was discontinued. Sulfapyridine was administered from the 4th to the 11th day in doses of 2.4 gm. every 24 hours. Left thoracentesis on the 5th day of illness yielded pus containing only Type 14 pneumococcus, and on the 16th day only Type 1 pneumococcus. Surgical drainage of the pleural cavity was established by a rib resection on the 18th day and the patient was discharged improved on the 42nd day of illness.

CASE 3. A boy of 9 months was admitted on the 9th day of illness with pneumonia in the left upper lobe and roentgenological evidence of fluid along the left axillary border and in the left costophrenic sinus. Type 14 pneumococcus was obtained from the sputum as well as from five cultures of the blood taken from the 9th to the 18th day of illness. On the 21st day *Staph. aureus* was present in a single blood culture, apparently as a contaminant. Cultures of the blood thereafter remained sterile. Massive empyema developed rapidly on the left and was partially drained by thoracentesis on the 13th day. Surgical drainage was established on the 16th day. Concentrated antipneumococcus Type 14 rabbit serum was given from the 9th to the 14th day, with only transient clinical improvement. The patient ran a prolonged and stormy course, complicated further by a septic left knee, which was drained surgically after 1 month's illness and yielded Type 14 pneumococcus in pure culture. Sulfapyridine was administered from the 36th to the 53rd day of illness. The patient was finally discharged in good condition after 3½ months of hospitalization.

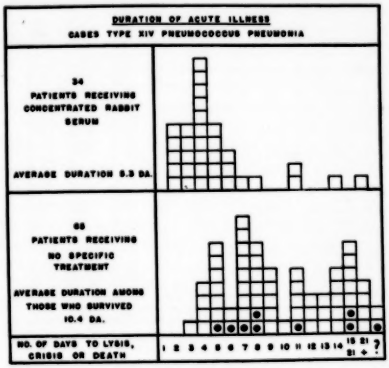
DURATION OF ACUTE ILLNESS
CASES TYPE XIV PNEUMOCOCCUS PNEUMONIA
34
PATIENTS RECEIVING CONCENTRATED RABBIT SERUM
AVERAGE DURATION 6.3 DA.
65
PATIENTS RECEIVING NO SPECIFIC TREATMENT
AVERAGE DURATION AMONG THOSE WHO SURVIVED 10.4 DA.
NO. OF DAYS TO LYSIS, CRISIS OR DEATH
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 21 ? 21 +

FIGURE 5.

Each square represents a case, and each dotted square a fatality.

The results of treatment with concentrated antipneumococcus Type 14 rabbit serum are perhaps most effectively demonstrated by comparing the patients who received this form of therapy with those who did not.

The duration of acute febrile illness for 99 of the 104* patients with pneumonia is represented in Figure 5. Among the non-serum-treated cases the average duration of acute febrile illness in the surviving patients for whom this could be estimated from the histories given was ten and a half days. In the group of 34 patients who received concentrated rabbit serum this period was

*The 3 patients who received unconcentrated rabbit serum and the 2 treated with sulfapyridine alone are not included in Figure 5.

reduced to five and a half days, and for the 31 patients who apparently were benefited to four and a half days. Eighty per cent of the serum-treated patients recovered after an illness of six days or less, whereas only 22 per cent of the non-serum-treated patients recovered in the same period. The long duration of acute illness in the untreated cases was accounted for in most cases not by complications but by continuation of the pneumonic process, with spread to other areas or failure to terminate by lysis or crisis.

TABLE 7. *Complications of Pneumonia in 104 Cases.*

COMPLICATION	NO. OF CASES	NO. OF RECOVERED CASES	DEATHS	POST-MORTEM EXAMINATIONS
Otitis media, non-suppurative	28	26	2	1
Otitis media, suppurative*	41	33	8	8
Mastoiditis	7	3	4	4
Empyema	5	3	2	2
Pleural effusion	4	1	3	3
Fibrinous pleuritis	3	0	3	3
Pulmonary abscess	5	1	4	4
Mediastinitis	4	0	4	4
Pyopneumothorax	1	0	1	1
Pericarditis	5	0	5	5
Toxic leukopenia	1	0	1	1
Tracheobronchitis	1	0	1	1
Jaundice	2	2	0	0
Focal necrosis of liver	1	0	1	1
Sinusitis with ethmoiditis	1	1	0	0
Meningismus	16	16	0	0
Encephalitis	1	1	0	0
Meningitis	2	0	2	2
Pyarthrosis	1	1	0	0

*Of the 41 cases with purulent otitis media, cultures were taken during life or at autopsy on 33; from 24 of these cultures, including 7 of the 8 patients who came to autopsy, Type 14 pneumococcus was obtained from one or both ears.

Complications (Table 7), with the exception of otitis media, which occurred in 66 per cent of all the cases, were relatively uncommon. In many patients otitis media was present at the time of hospitalization and it was impossible to determine whether the otitis occurred as a complication of pneumonia or as a manifestation of preceding upper respiratory infection. Serious complications, although infrequent, almost invariably proved fatal in non-serum-treated patients and did not occur in those receiving concentrated serum, save in the 2 patients previously mentioned (Cases 2 and 3), who had empyema at the time antipneumococcus Type 14 serum was first administered.

Pneumococcus Type 14 was grown from the blood of 8 (9 per cent) of the 86 patients with pneumonia from whom cultures were taken during life (Table 8). The 2 infants who received concentrated serum survived, although 1 of them (Case 3) failed to show any immediate benefit in response to serum administration. Two infants who were not treated with concentrated serum, 1 of whom received unconcentrated serum, died. Of the 4 children over two years of age in whom cultures of the blood were positive, none received concentrated serum and 1 died. One of the patients who survived was treated with sulfapyridine.

Among the 70 patients who were not treated with concentrated rabbit serum there were 10 deaths, including 1 of the 3 patients who were given unconcentrated serum early in 1937. Nine of the 10 patients who died were studied at autopsy, and pneumococcus Type 14 was the predominant pathogen obtained from cultures of the blood, lungs and purulent exudates in all but the 2 patients mentioned previously. In the 1 fatal case which did not come to autopsy, pneumococcus Type 14 was the only organism of significance recovered during life. All the fatal cases examined postmortem had purulent complications secondary to the acute pneumonic process.

The mortality rate in untreated patients, reduced to its lowest terms by exclusion of cases in whom other organisms appeared to be of greater significance (Table 4), and those receiving other forms of specific therapy, was 15 per cent for 34 infants under two years of age and 7 per cent for 27 children over two years of age. Among the 34 patients who received concentrated rabbit serum, 22 of whom were infants under two years of age, there were no fatalities.

TABLE 8. *Analysis of Deaths from Pneumonia.*

CLASSIFICATION OF CASES	TOTAL NO. OF CASES	DEATHS	MORTALITY %	INFANTS (UNDER 2 YR.) NO. OF CASES	INFANTS (UNDER 2 YR.) DEATHS	INFANTS (UNDER 2 YR.) MORTALITY %	CHILDREN (2–12 YR.) NO. OF CASES	CHILDREN (2–12 YR.) DEATHS	CHILDREN (2–12 YR.) MORTALITY %
Cases occurring prior to use of concentrated antipneumococcic rabbit serum	58[5]*	10[3]	17	36[2]	8[2]	22	22[3]	2[1]	9
No specific treatment	55[5]	9[3]	16	34[3]	7[2]	21	21[2]	2[1]	10
Unconcentrated rabbit serum	3[1]	1[1]		2[1]	1[1]		1	0	
Cases occurring after March 21, 1938	46[3]	0	0	27[2]	0	0	19[1]	0	0
Treated with concentrated rabbit serum	34[2]	0	0	22[2]†	0	0	12	0	0
Treated with sulfapyridine alone	2[1]	0	0	1	0	0	1[1]	0	0
No specific treatment	10	0	0	4	0	0	6	0	0

*Superscripts indicate the number of cases from which positive blood cultures for pneumococcus Type 14 were obtained during life.
†Concentrated antipneumococcus Type 14 rabbit serum was given to 1 infant who had received sulfapyridine for 48 hours without improvement.

COMMENT

The Type 14 pneumococcus appears to have its highest incidence and greatest pathogenicity among infants and young children in whom it is the dominant pneumococcal agent of pneumonia. When found in patients of this age group even when associated with other organisms it is usually of etiologic importance in relation to existing pulmonary infection, and it has not been found to occur commonly in the absence of pulmonary infection. As a cause of pneumonia in patients of pre-school age its importance is comparable to that of the Type 1 pneumococcus in adults.

In infants and young children, pneumonia attributable to the Type 14 pneumococcus is usually a severe and prolonged disease. Even with hospital care and good supportive treatment the fatality rate has been relatively high, particularly in patients under two years of age.

Favorable results with the use of horse serum in the treatment of Type 14 pneumococcus pneumonia in infants and children have been reported.[3, 4, 12–14] Recent investigations into the cause of unusual and sometimes fatal reactions in occasional patients receiving antipneumococcus Type 14 horse serum led to the observation that the serums of horses immunized against Type 14 pneumococci have agglutinins in high titer for human erythrocytes of all four blood groups.[15] In view of these findings the use of available antipneumococcus Type 14 rabbit serums of equal or greater potency which do not possess this property is preferable. Furthermore, rabbit serum may be given safely to patients sensitized to horse serum by previous immunization, and conversely, administration of rabbit serum will not sensitize to horse serum, which may be indicated subsequently for other purposes.

Indiscriminate utilization of serum therapy for mildly or moderately ill children with pneumonia has been wisely discouraged by Nemir,[14] who recommends its use only for severely ill patients early in the course of their disease and for infants in whom the mortality is high. However, as all pneumococci do not produce pneumonia of like severity and the early clinical appearance of an individual patient may prove deceptive with respect to his ultimate course, the pneumococcus type responsible is another important factor to be taken into consideration. The finding of Type 14 pneumococcus in an infant or young child with definite pneumonia is in itself an indication for specific therapy.

Recent published and unpublished experiences with sulfapyridine in the treatment of pneumonia have indicated that this new chemotherapeutic agent may have a wide range of usefulness, especially for infants and children. As most of the present group of patients were treated before sulfapyridine became available, no further comment is within the scope of this report other than to emphasize the importance of accurate bacteriological diagnosis for achieving a proper evaluation of its effectiveness.

The 34 patients here reported to whom concentrated antipneumococcus Type 14 rabbit serum was administered were selected as suitable for this treatment from 46 consecutive patients with pneumonia from whom pneumococcus Type 14 had been isolated. Serum was introduced not to substitute for supportive measures of well-established value but to supplement them in an effort to achieve a more effective course of treatment. Although the number of patients who received the concentrated type-specific rabbit serum is small and the non-serum-treated cases analyzed do not represent a properly constituted control, comparison of these two groups affords a basis for tentative conclusions. From the clinical results obtained, concentrated antipneumococcus Type 14 rabbit serum, administered in relatively small doses, appeared to be of definite therapeutic value.

SUMMARY AND CONCLUSIONS

In a series of 120 infants and children, including 104 with pneumonia from whom Type 14 pneumococcus was cultured, the salient clinical and bacteriological findings have been presented and discussed.

Concentrated antipneumococcus Type 14 rabbit serum was administered to 34 of the patients with pneumonia, including 22 under two years of age.

All the patients who received this form of therapy survived, and all but 3 with complications or mixed infection showed prompt improvement in response to adequate doses.

The clinical results obtained indicate that for the treatment of pneumococcus Type 14 pneumonia in infants and children, concentrated antipneumococcus Type 14 rabbit serum constitutes a valuable addition to the usual modes of therapy.

The author acknowledges his indebtedness to members of the clinical and bacteriological staffs whose cooperation made this study possible, to Dr. Maxwell Finland, of the Boston City Hospital, for his helpful suggestions, to Mrs. Christina Came for her assistance in preparing the charts and tables and to Dr. W. G. Malcolm, executive director of the Lederle Laboratories, Incorporated, Pearl River, New York, who generously provided the therapeutic serums.

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THE TREATMENT OF PNEUMOCOCCAL PNEUMONIA IN INFANTS AND CHILDREN WITH SULFAPYRIDINE*

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THE advent of sulfapyridine[1] for the treatment of infections due to the pneumococcus and other organisms came at a time when specific anti-pneumococcus serums, including those recently developed against many of the more important higher types of pneumococci (Types 4 to 32) so frequently associated with the pneumonia of infants and children,[2] were fully justifying their employment on a large scale. Therefore, when sulfapyridine was first introduced at the Infants' and Children's hospitals in Boston in October, 1938, the new drug was administered to only a few carefully selected patients for whom type-specific serum was not available. Their response was so satisfactory that, during the period from December, 1938, to June, 1939, when this study ended, sulfapyridine displaced serum entirely in the treatment of pneumonia due to pneumococci of all types.

The criteria adopted for the employment of sulfapyridine were definite clinical evidence of pneumonia not already in the convalescent stage and the presence of one or more types of pneumococci in the patient's throat. In all, 154 patients with pneumococcal pneumonia—71 infants and 83 children—were treated with sulfapyridine during this period (Table 1). The pneumonia was considered primary in 151 patients.

TABLE 1. *Patients with Pneumococcal Pneumonia Treated with Sulfapyridine.*

	INFANTS	CHILDREN
Male	43	48
Female	28	35
Totals	71	83
Average age	10.5 mo.	4.6 yr.

*From the Infants' and Children's hospitals, Boston, and the Department of Pediatrics, Harvard Medical School.

†Associate in pediatrics and instructor in bacteriology, Harvard Medical School; associate visiting physician and staff bacteriologist, Infants' and Children's hospitals.

Physical signs of pneumonia in practically all the patients were confirmed by fluoroscopic examination on the ward by one of the hospital residents, and x-ray films of the lungs were taken routinely within twenty-four hours after admission. Only one of the patients in this series received neither examination. The extent of the consolidation in the lungs of all but 15 was noted by both x-ray and fluoroscopic examinations, repeated according to the condition of the patient.

At first only those patients were treated with sulfapyridine from whose throats a typed pneumococcus had been obtained. Later, sulfapyridine was administered to very ill patients on the presumptive evidence that the demonstrated pneumonia was due to the pneumococcus. Treatment was continued only if this impression was confirmed by Neufeld typing of material from the patient.

BACTERIOLOGICAL STUDIES

Material for pneumococcus typing was obtained by placing a sterile swab deep in the patient's pharynx and inducing a cough. A tube of sterile ascitic fluid was inoculated from this swab and incubated for from four to six hours. During this period the pneumococci usually outgrew the other organisms, and it became possible to recognize them and determine their specific types by the Neufeld method (capsular swelling). Occasionally the material from the throat contained enough pneumococci to permit immediate typing.

In this series a justifiable distinction is drawn between infants and children, for the two groups tend to differ not only immunologically,[3-5] but also in respect to the predominant types of pneumococci found in their throats, as well as in their clinical response to infection by these organisms.

Among the infants under two years of age, for example, Type 14 was by far the commonest, Types 7, 19, 3 and 6, and 4 and 17 following in that order. Types 1 and 2 were not encountered among the infants, but all the other types through Type 29, except Types 13, 24, 25 and 28, were found at least once. In the children over two years of age, Type 1 was predominant. Type 14

TABLE 2. *Incidence of Multiple Types of Pneumococci in the Same Patient.*

NO. OF TYPES	INFANTS	CHILDREN
1	51	48
2	16	18
3	4	13
4	1	3
5	0	0
6	1	0
7	0	1
Totals	73	83

was the next most frequent, occurring especially among the younger children. Then came Types 19, 6 and 7, and, all with equal frequency, 3, 10, 16 and 23. The new "Wilder"[6] strain occurred in 3 children.

In 30 per cent of the infants and 43 per cent of the children more than one type of pneumococcus was recovered from the throat at the same time (Table 2).*

Since other pathogenic organisms, such as *Staphylococcus aureus, Streptococcus hemolyticus* and *Hemophilus influenzae,* may invade the lungs along with pneumococci or independently, a blood agar plate was inoculated from a "deep throat swab." Although other pathogenic organisms were frequently encountered in such cultures (Table 3), their role was not always clear. In

TABLE 3. *Organisms Accompanying Pneumococci in Throat Cultures.*

ORGANISMS	INFANTS	CHILDREN
Streptococcus hemolyticus	16	19
Staphylococcus aureus	9	4
Str. hemolyticus and *Staph. aureus*	2	0
Hemophilus influenzae	0	6
Str. hemolyticus and *H. influenzae*	0	1
Totals	27	30

at least two instances, however, they seemed to contribute to the fatal outcome, since they were present in the blood stream before death.

The blood cultures of 13 patients were positive (Table 4). All but 3 patients had a blood culture taken before sulfapyridine therapy was started. In no case did the blood culture remain positive for pneumococci after the administration of sulfapyridine.

*Credit for the success in finding these numerous types of pneumococci is due the painstaking work of Dr. W. I. Francke, Dr. F. H. Allen, Dr. C. G. Grulee, and Miss Marian Sweet, in the Bacteriology Laboratory, Children's Hospital.

OTHER LABORATORY PROCEDURES

Complete blood counts and urinalyses were done on admission and an attempt, only partially successful, however, was made to repeat these at least every three days. Recently a daily urinalysis as long as the drug is administered and for three days thereafter has been the rule. In most instances the concentration of sulfapyridine in the blood was determined during the height of fever and during convalescence, a convenient micromethod[7] being used which required only 0.1 cc. of blood from a finger or toe.

TREATMENT

Supportive

On admission to the hospital immediate steps were taken to make the patient as comfortable as possible. General supportive measures suited to the particular patient were adopted. Three infants were placed in an oxygen tent soon after admission. Five received blood transfusions at some time during their stay in the hospital. All

TABLE 4. *Positive Blood Cultures.*

ORGANISMS	AGE	OUTCOME
	yr.	
Pneumococcus		
Type 1	2 4/12	Died in 2 mo.
Type 1	3, 8 2/12	Recovered
Type 4	1, 1 4/12, 1 5/12	Recovered
Type 14	6/12, 1 1/12, 1 3/12, 1 5/12, 2 10/12	Recovered
Streptococcus hemolyticus	8/12	Died
Staphylococcus aureus	2/12	Died

infants and children who were in a state of ketosis or dehydrated from vomiting or diarrhea or insufficient fluid intake were given intravenous glucose and saline solutions. Morphine and the barbiturates were not withheld when the patient was in pain or restless. Enemas were given and rectal tubes were used for abdominal distention.

Sulfapyridine

Sulfapyridine† is a white, almost tasteless, crystalline substance,[8] relatively insoluble in water. Except in a few instances, the drug was administered by mouth in powdered form, mixed with a palatable semisolid food, such as apple sauce or junket, as a vehicle. The sodium salt of sulfapyridine[9] is very soluble in water and may be given intravenously in a concentration of from 1 to 5 per cent, but owing to its alkaline reaction (pH 10 to 11) it is not suitable for subcutaneous injection in these concentrations. Three patients in this series received one or more intravenous injections of the sodium salt of sulfapyridine. In most cases, sulfapyridine was readily absorbed by mouth. By rectum the absorption

†The sulfapyridine used in this study was supplied through the courtesy of the Calco Chemical Company, Incorporated, Bound Brook, New Jersey, and the Lederle Laboratories, Incorporated, Pearl River, New York.

was found to be irregular and as a rule insufficient for the best therapeutic results. In agreement with the experience of others,[10] a blood level of 4 to 8 mg.* per 100 cc. appeared to be desirable. In 3 patients the above routes of administration were combined.

Most of the infants were given an initial dose equal to about ⅓ or ½ gr. of sulfapyridine per pound of body weight, and thereafter 1½ gr. per pound per day, in four to six divided doses. Children were given a similar initial dose and thereafter 1 gr. per pound per day in divided doses. As a general rule, the drug was discontinued after the temperature had been normal for two or three days or until some complication rendered further therapy with sulfapyridine inadvisable. Sodium sulfapyridine in normal saline solution was given intravenously in a dose of ½ gr. per pound in a single case, and in a dose of 1 gr. per pound in two others. The sodium salt was not given rectally.

Clinical Results

The regularity of the clinical response to sulfapyridine was very impressive. Of the 71 infants treated with sulfapyridine (including 1 treated twice and 2 re-admitted), 57 (80 per cent) became afebrile within forty-eight hours, 19 (27 per cent) in the first twelve hours and 19 (27 per cent) more in the next twelve hours. Of the 9 who improved more slowly, over a period of two to six days, 2 had purulent otitis media, 1 had amyotonia congenita, and 1 received an insufficient dose. Five infants died, all under circumstances such that the outcome could not have been ascribed solely to the failure of sulfapyridine (Table 5).

Table 5. *Data on Infants Who Died.*

TYPE OR TYPES OF PNEUMOCOCCI IN THROAT	AGE	COMPLICATIONS
	mo.	
Type 21	2	*Staphylococcus aureus* septicemia and abscesses of lungs (autopsy)
Types 11, 16 and 27	4	Agenesis of the right lung (autopsy)
Type 12	4	Eczema and abscesses of the scalp
Types 6, 8 and 19	8	Amyotonia congenita and *Streptococcus hemolyticus* septicemia (autopsy)
Types 4 and 6	12	Died less than 4 hours after admission

Of the 79 children, excluding 4 who were essentially afebrile or apparently convalescent at the outset of therapy, 71 (90 per cent) became afebrile within forty-eight hours after sulfapyridine was first administered, over half of these within twenty-four hours. Of the 3 who did not become afebrile until sixty hours had elapsed, 2 suffered from chronic bronchitis. Of the four whose fever persisted for longer periods (up to six days), 1 child had a plastic pleural exudate and 3 had empyema. The only fatality among the children was a little girl of two and a half years. She was moribund on admission. An emergency thoracentesis was done because of a massive empyema. She developed bilateral pneumothorax and empyema and died after a lingering illness of two months.

There was no apparent correlation between the length of time the patients had been acutely sick before sulfapyridine was begun and the speed with which they responded to the drug, or between the type of pneumococcus and the character of the response.

Although otitis media was present in an undetermined number of the infants (Table 6), and although several patients had pleurisy and empyema, there was evidence in every case that the complications were present, at least in their incipiency, at the time that sulfapyridine therapy was begun. For example, when empyema developed, the admission examination, by physical signs or x-ray, had disclosed thickening of the pleura on that side of the chest or even pleural fluid. With one exception, an infant with Type 14 infection, those patients with frank empyema eventually required operation, in spite of aspiration of the pus and the continued administration of sulfapyridine.

Table 6. *Complications.*

COMPLICATION	INFANTS	CHILDREN
Otitis media or mastoiditis, or both	?	10
Thickened pleura	9	8
Plastic pleural exudate	0	2
Sterile pleural fluid	0	3
Empyema	1* (no operation)	4† (operation)

*Type 14 pneumococcus.
†Three with Type 1 pneumococcus, one with Types 1 and 7.

Provided no frank complication was present, the children, once convalescent, usually went on to prompt and complete recovery with the subsidence of the fever. One girl of four and a half years, who responded rapidly to the usual dose of sulfapyridine, was known to have a plastic pleural exudate at the base of the right lung. She was discharged home for further convalescence, but returned twenty-four hours later with a moderate fever. This subsided in two days without the aid of sulfapyridine and the signs of pleural thickening gradually disappeared.

On the other hand, 6 infants exhibited a persistence of the infection or a re-infection in the same parts of the lungs first involved, the sulfapyridine having been discontinued because of apparently satisfactory convalescence. The signs

*Unconjugated sulfapyridine.

of activity in the lungs reappeared at various intervals. Brief case histories are as follows:

Case 1. L. N., a 15-month-old boy, was admitted with pneumonia in left lower lobe and some pleural reaction over the left lung. Types 6, 7 and 19 pneumococci were recovered from the throat. He responded quickly to sulfapyridine and was sent home in 10 days.

Ten days later he was re-admitted with fever and evidence of bronchitis. Types 6 and 7 pneumococci were found in the throat. He recovered without sulfapyridine therapy and was discharged in 6 days.

On a third admission 4 months later there were signs of pneumonia in the left lower lobe. Types 5, 7 and 19 pneumococci were recovered from the throat. He responded rapidly to a single large dose of sulfapyridine and was sent home in 7 days.

Case 2. B. S., an 8-month-old girl, was admitted with the diagnosis of amyotonia congenita and pneumonia in the right upper lobe. Types 6, 8 and 19 pneumococci were recovered from the throat. There was a slow response (afebrile in 88 hours) to sulfapyridine. She was discharged after 37 days, with the lungs apparently clear.

She was re-admitted 10 days later with signs of pneumonia in the right upper lobe. Type 19 pneumococci and hemolytic streptococci were found in the throat. Sulfapyridine was started but she died on the 2nd day, with hemolytic streptococci in the blood culture.

Case 3. G. T., an 8-month-old girl, was admitted with a diagnosis of bronchopneumonia. Type 22 pneumococci were found in the throat. There was a rapid response to sulfapyridine. She was discharged, apparently well, after 14 days.

She was re-admitted after 10 days at home, with bronchopneumonia. Type 22 pneumococci were still present in the throat. There was again a rapid response to sulfapyridine, and she was discharged 13 days later.

Case 4. W. T., an 11-month-old girl, was admitted for pneumonia in the left lower lobe. Types 21 and 23 pneumococci were found in the throat. There was an excellent response to sulfapyridine, and she was in the hospital only 9 days.

She was re-admitted 17 days later, with pneumonia in the left lower lobe. Types 7, 14, 19 and 23 pneumococci were recovered from the throat. She responded well to a second course of sulfapyridine and was sent home after 9 days.

Case 5. E. K., a 6-month-old girl, was admitted with the diagnoses of interstitial pneumonia and a pleural reaction at the base of the right lung. A Type 14 pneumococcus was found in the throat. A blood culture was positive for Type 14 pneumococci (500 to 1000 colonies per cubic centimeter). The right knee was swollen, and pus aspirated from it yielded Type 14 pneumococci. The knee was drained surgically and healed promptly. She was transfused four times.

Four courses of sulfapyridine, lasting 14, 18, 18 and 3 days respectively, were given. Each time she responded to the drug with a rapid fall of temperature to normal, but 3 to 5 days after the end of each of the first three courses, when the amount of sulfapyridine in the blood had fallen to a very low level, her fever returned and, except for the last bout of fever, her blood culture became positive for Type 14.

Finally, a small amount of pus containing Type 14 pneumococci was aspirated from the right pleural cavity. She thereupon made a rapid recovery.

Case 6. This girl, G. B., developed pneumonia from aspiration of vomitus on the second day of life and was given sulfapyridine at another hospital. She was discharged on the 12th day and admitted to the Infants' Hospital at the age of 3 weeks, with pneumonia and some atelectasis of the right upper lobe. Type 3 pneumococci were found in the throat. Because of her precarious condition no blood culture was taken.

Sulfapyridine was given for 7 days. Her fever subsided in 48 hours, but 2 days after discontinuing sulfapyridine her temperature rose to 103.4°F. and Type 3 pneumococci were again found in the throat. After the institution of a second course of sulfapyridine, lasting 7 days, her temperature returned to normal in 12 hours.

Three days after discontinuing sulfapyridine a second time her fever returned, but subsided without the aid of the drug. After a month at home she was re-admitted to the hospital with bronchitis. Many Type 5 and a few Type 3 pneumococci were found in the throat. No sulfapyridine was given, and she was discharged in 10 days. An x-ray film of her lungs 2 months after the first admission still showed slight infiltration of the right apex and peripheral emphysema.

Toxicity of Sulfapyridine

A new drug is judged not only by its efficacy in assisting the patient to combat a disease, but also on its relative safety. Sulfapyridine is undoubtedly a toxic drug, as evidenced by the incidence of untoward reactions. Of these, vomiting was most frequently experienced in this series (Table 7). It is difficult to appraise accurately the relation of this symptom to sulfapyridine, since so many infants and children with pneumonia vomit even before the drug is given. Most patients showed some loss of appetite and were quite irritable as long as they took the drug. Some stopped vomiting while still receiving sulfapyridine. In keeping with the observation that the concentration of the drug in the blood usually fell to very low levels within forty-eight hours after discontinuing it, the toxic symptoms almost always cleared within a day or two after the drug had been stopped.

Table 7. *Toxic Manifestations of Sulfapyridine.*

Symptom or Sign	Infants (71)	Children (83)
Nausea	10	4
Vomiting	21	29
Hematuria	1	3*
Rash	0	1
Cyanosis	0	1
Anemia or leukopenia	0	0
Drug fever	0	2 (?)

*Cleared in 2, 2 and 4 days respectively.

The most alarming sign encountered was hematuria (Table 8), which came on abruptly in 4 patients, with some pain in the region of the kidneys in 1. Sodium bicarbonate by mouth and parenteral fluids designed to flush the kidneys were administered. In none was the symptom

severe, and all the patients recovered, with no apparent residual renal damage.

Discussion

The experience gained from the treatment of this series of infants and children and from the experience of others[10-12] does not as yet enable one to state categorically the optimum dosage and method of administration or to define exactly the full potentialities and the limitations of the drug. It is quite evident, however, that in sulfapyridine an extraordinarily effective agent for the treatment of pneumonia due to pneumococci has been developed. Sulfapyridine has certain advantages over type-specific serums:—

Table 8. *Data on Cases with Hematuria.*

Age	Day after first dose	Blood level	Cleared
yr.		*mg. per 100 cc.*	*days*
5/12	3	9.2 (3rd day)	<7
2 3/12	5	?	2
5 9/12	6	5.4 (3rd day)	2
2 6/12	3*	11.8 (1st day)	4

*Received large dose first day, none thereafter.

1. It is easily administered by mouth (as a rule it does not require venipuncture).

2. With rare exceptions,[13] it is apparently effective against all strains of pneumococci. This property obviates the need for having available numerous type-specific antipneumococcus serums. When multiple types of pneumococci are present in the throat of the same patient at the same time, one need not attempt to select the most likely type for serotherapy.

3. Its period of greatest effectiveness is not limited to the early stages of pneumonia.

4. It may be given to allergic and serum-sensitive patients. The condition of desperately sick patients is not made more precarious by thermal reactions so common after serum therapy. Except for rare cases, it may be given repeatedly at various intervals.

5. It is also effective against hemolytic streptococci.[14]

6. It is relatively inexpensive.

Granting these general advantages of sulfapyridine over serum, the risk of toxic reactions, such as hematuria,[15] granulocytopenia[16] and acute hemolytic anemia,[17] indicates that the use of the drug should be reserved for those infants and children with definite pneumonia due to pneumococci (or hemolytic streptococci) where the severity of the illness justifies the hazards of chemotherapy, slight though these appear to be.

Surgical complications, where vomiting would be detrimental, the failure of the patient to respond to sulfapyridine, or a known idiosyncrasy or untoward reaction to the drug may now and then call for serotherapy. Furthermore, the possibility that selected cases would profit by the combined use of serum and sulfapyridine must be borne in mind.[13]

Recommendations

An initial dose of ½ gr. of sulfapyridine per pound of body weight, by mouth, followed by small divided doses amounting to 1 gr. per pound per day for children and 1½ gr. per pound per day for those under two years of age, usually results in therapeutically effective blood levels (4 to 8 mg. per 100 cc.). The drug should be mixed with some semisolid food. At the outset, inability of the patient to retain the drug by mouth or the severity of the illness may occasionally require the intravenous administration of sodium sulfapyridine in a 5 per cent concentration in sterile distilled water, in a dose of ½ or 1 gr. per pound. This should be given slowly, with great care not to allow extravasation of fluid from the vein. Intravenous sodium sulfapyridine may be repeated in six or eight hours; but an immediate attempt should be made to have the patient take the ordinary form of the drug by mouth, and in no case should the intravenous administration be continued without determining the concentration of the drug in the blood at frequent intervals.

Failure of the patient to respond favorably within forty-eight hours is an urgent indication not only for a determination of the blood level of the drug as a guide to possible alterations in the dosage, but also for a review of the case as to diagnosis, and especially for a careful search for complications, such as empyema. In uncomplicated cases it is usually advisable to discontinue the drug after the temperature has been approximately normal for one or two days. Under no circumstances should the continuance of the drug in the presence of known complications be allowed to mask the indications for surgical drainage.

Because of possible toxic reactions, a complete blood count at least every three days during the administration of the drug and a daily urinalysis as long as the drug is administered and for three or four days thereafter are strongly advised.

When sulfapyridine is continued for more than two or three days a determination of the blood level will serve as a guide to the daily dosage. Intelligent understanding of the case calls for a blood culture and an examination of material from the patient's throat for pneumococci and for other pathogenic organisms, since the latter may

impose their own characteristic features on the course of the disease.

Success with specific measures for the treatment of pneumonia in infants and children has lessened the burden of nursing care and general supportive measures, but the latter are still of fundamental importance. The most effective combination of all the measures suited to the needs of the individual patient still calls for the practice of the art of medicine.

SUMMARY

An analysis of 154 sulfapyridine-treated cases of pneumococcal pneumonia in infants and children is presented, with certain recommendations.

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Discussion of Papers by Drs. McDonald, Curnen and Davies

Dr. Maxwell Finland, Boston: All the problems bearing on treatment of pneumonia are much the same in children and in adults, except that they are dealt with in a somewhat special manner. The major problem was well summarized in Dr. Davies's last words, which very aptly covered the whole subject. It is important that in the treatment of pneumonia in children the emphasis be not entirely focused on drug therapy, thus eclipsing completely all notion of the care of the patient, and ignoring the fact that there are beneficial methods of treatment which have to be borne in mind at some time or other, regardless of how valuable or important any given effective agent is. It is essential to bear in mind that the patient must be treated, and that, since under certain circumstances a particular remedy may not be effective, it is well to be acquainted with other tried remedies and to be in a position to use them effectively when the time comes.

Dr. McDonald's presentation of the results from the Floating Hospital, which showed a striking drop in the death rate with the introduction of transfusion and oxygen therapy, plus, of course, the improvement in the general treatment of the children, is highly significant. To attain a mortality of only 2 per cent in 73 patients under two years of age is quite an achievement, considering all the high death rates in that age group which the speaker has cited from the literature, and which are becoming more and more evident as physicians type their cases and evaluate the death rate on the basis of etiologic agents. We recognize that Type 14 pneumococcus is an important one in children under two, and this particular group has a considerable mortality.

The underlying factors concerning the effective agents in transfusion are very difficult to perceive. No doubt the nutritional value and the oxygen-carrying property of the blood, and perhaps other factors, are important. One interesting feature in which I am particularly interested has been the fact that the Type 14 pneumococcus, as you have seen from Dr. Curnen's chart, is not a very prominent type in older children, and in adults rarely occurs as the cause of pneumonia. Along with this we find that while infants may have some slight basic immunity to pneumococcus Type 14, adults almost universally have a high grade of immunity. It is very difficult to find 0.5 cc. of blood from an adult which when mixed with virulent Type 14 pneumococci is unable to destroy hundreds of thousands of bacteria in a very short time. When such blood is introduced into the infant it may have some bearing on the outcome, and some of the dramatic crises following transfusions may very well be attributed to that particular property of adult blood.

The demonstration that Dr. Curnen gave of the efficacy of antipneumococcus serum, entirely apart from whether it is the preferred treatment, is certainly impressive and warrants consideration. These results were obtained with rabbit serums. These serums, we must bear in mind, have only recently been perfected so that reactions are becoming very uncommon, particularly the severe, allergic, and perhaps fatal type. Even thermal reactions are becoming much less frequent. The serums are now highly potent and highly concentrated. In practically all types they are considerably more effective than before, and dramatic responses are more frequent.

In serum-treated patients there are a minimum of reactions, aside from serum sickness. The latter bothers us very little because it occurs when the patient is well. Usually, as Dr. Curnen has pointed out, serum sickness is very easy to treat and we do not worry about it. The dangerous reactions from serum occur while one is treating the patient and is prepared to meet them. This is a factor to be borne in mind, particularly if one is treating a patient in the home. Complications of drug therapy such as hematuria, anemia and granulocytopenia may be insidious in their onset, and are likely to appear in patients who are not yet well. The physician may be unable then to differentiate symptoms of pneumonia and those due to the drug. These complications may appear in the intervals between blood counts or urine analyses, and drug therapy may be continued in the meantime to the detriment of the patients. We have seen, and others have described, patients who have developed nitrogen retention and generalized edema and have died with concretions of acetylsulfapyridine crystals in their kidneys.

The fact that untoward effects occur should not deter us from using these valuable life-saving measures; but

the toxic effects of the drugs must be borne in mind even in young children, and in spite of the fact that, in general, infants and children tolerate the drug considerably better than do adults.

The fact that some infants and some older children still die from pneumonia does not mean that these particular drugs are not effective. With all important life-saving measures such as specific serums and sulfapyridine there will always be a certain number of deaths. These will occur under unusual conditions, that is, in patients who are neglected and come to treatment late, or in those who have already developed complications of the disease which are not adequately affected by either specific serum therapy or drug therapy. Therefore early diagnosis and the advisability for parents to call physicians as soon as possible are just as important or perhaps more important now than ever before, because we have much to offer. The main thing we have to bear in mind is that we still have to treat our patients and still have to study them. Diagnostic problems, particularly in the course of treatment, have increased rather than decreased as compared with what they were before we had specific serum, and particularly before we had the new chemicals.

A PHYSICIAN: I should like to ask Dr. Davies whether he always uses sodium bicarbonate.

DR. DAVIES: We have no rule about it. In some cases we give sodium bicarbonate, in others we do not.

DR. JAMES M. BATY, Boston: I should like to ask Dr. Davies if at the Children's Hospital sulfapyridine is continued five or six days. Dr. Charles H. Smith, of New York City, reported at a recent meeting that they had arrived at the point of continuing its use only two or at the most three days, and if the temperature was normal or practically normal at that point they omitted the drug and did nothing else. If the temperature was still elevated and the patient was apparently not responding, they omitted the drug and gave specific serum if it was available.

DR. DAVIES: It is probably best to continue the drug for two or three days or at least until the temperature has not only reached normal but has remained normal for about twenty-four hours.

DR. BATY: Dr. Finland, have you studied the development of antibodies following the giving of sulfapyridine?

DR. FINLAND: Yes, we have studied this aspect extensively. In adults, so far as we have been able to ascertain, the development of immunity is the same in patients who have been treated with sulfapyridine as in those who have received no specific therapy. Many develop or have antibodies early, but in some cases the first demonstrable antibodies appear as late as the fourteenth day of illness. Occasionally the patient's temperature has already been normal for a week before specific antibodies are first demonstrated. In some patients relapses of fever have occurred. We have not yet correlated our findings, but relapses of fever, although they do occur, are not so frequent as one might expect from the delay in the development of immunity. It may be that antibodies which are not demonstrated by protection tests are adequate, or else some other mechanism of recovery is involved.

A PHYSICIAN: Dr. Davies, have you cured any cases of pneumococcal peritonitis?

DR. DAVIES: In the past year we have had, I think, two cases which recovered. I think Dr. Curnen can tell you more about them.

DR. CURNEN: The one patient I remember who had pneumococcal peritonitis and received sulfapyridine did not provide a satisfactory test of the drug's effectiveness. Pneumococcus Type 6 peritonitis and bacteremia developed suddenly as a complication of nephrosis. The child's treatment included, successively, incision and drainage of the peritoneal cavity, a transfusion with blood subsequently found to possess type-specific antibodies, administration of sulfapyridine and intravenous injection of concentrated type-specific rabbit serum. Prior to the first dose of sulfapyridine the patient appeared to be clinically improved, the temperature had fallen and cultures of the blood had become sterile. The prompt recovery was gratifying, but proved inconclusive with respect to the individual merits of the several therapeutic agents used.

A PHYSICIAN: I should like to ask Dr. Davies to review the dosage of sulfapyridine.

DR. DAVIES: I think our dosage is somewhat similar to that employed elsewhere. The initial dose is ⅓ to ½ gr. per pound of body weight. The subsequent maintenance dose for infants is 1½ gr. per pound per day in four to six divided doses, and for children 1 gr. per pound per day, also in divided doses. In general, we continued the drug about two or three days after the temperature had become normal.

FURTHER STUDIES ON THE PERSONALITY AND SOCIOLOGICAL FACTORS IN THE PROGNOSIS AND TREATMENT OF CHRONIC ALCOHOLISM*

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IN A study reported by us[1] two years ago a preliminary attempt was made to survey systematically the sociological and personality characteristics of 120 alcoholic patients and, in 43 cases where adequate information was available, to determine whether any correlation could be discerned between the personality of an alcoholic patient and the ultimate results of his treatment in a mental hospital of the McLean type. Certain suggestive trends appeared to emerge from this preliminary study. "On the one hand," it was stated, "there is the patient who tends to do well: young (under thirty-five years of age), in good physical health, with a history of heavy drinking of less than seven years' duration, adaptable, energetic, capable of leadership, perhaps egotistical, possibly more attached to his father than to his mother, and in circumstances where a hospital residence of four months or more is feasible. On the other hand there is the patient whose prognosis is poor: older than forty years of age, in poor physical health, a heavy drinker for fifteen years or more, anergic, little ability to adapt himself to new situations, lacking in self-confidence, possibly strongly attached to his mother and remaining under treatment for only two and a half months or less." These tentative conclusions seemed sufficiently promising to justify further pursuit of the determinants of prognosis in chronic alcoholic patients treated in a mental hospital.

The present study attempts to find answers or hints of answers to the following two general categories of questions: First, is there an alcoholic type of personality? Are there individuals who are more or less predestined because of some special set of personality or sociologic characteristics to become addicted to the excessive use of alcohol? Current authoritative opinion[2] would seem to indicate that such is the case. If so, can those characteristics be accurately defined? And secondly, what role can the private mental hospital of the McLean type play in the treatment of chronic alcoholism? Is there a type of alcoholic patient, possessing this or that set of personality or sociologic traits, to whom the mental hospital offers the best outlook for recovery? If so, what are those favorable prognostic signs and, contrariwise, what are the traits which carry implications of poor prognosis in such a therapeutic setting?

This paper is based on an analysis of the sociological and personality findings in 124 alcoholic patients (100 men, 24 women) the results of whose treatment at McLean Hospital are accurately known. Each of the cases included in this series was selected as satisfying both of the following criteria: the patient's excessive use of alcohol was the immediate or principal cause for admission to the hospital; reliable and specific follow-up data were available as to what happened to the patient after his discharge from the hospital, with particular regard to the use of alcohol. This information was obtained in most cases by a trained social worker who visited the patient's family and obtained a first-hand contact; often data about a single case were obtained from multiple sources.§

TABLE 1. *Final Hospital Diagnoses in All Cases.*

	MEN	WOMEN
Chronic alcoholism without psychosis	61	14
Chronic alcoholism associated with psychopathic personality	13	3
Chronic alcoholism associated with drug addiction	3	3
Chronic alcoholism associated with pathologic intoxication	2	0
Alcoholic psychosis:		
Delirium tremens	4	0
Acute alcoholic hallucinosis	5	1
Manic-depressive psychosis associated with chronic alcoholism	6	1
Paranoid condition associated with chronic alcoholism	1	2
Korsakoff's psychosis	1	0
Other psychoses (cerebral arteriosclerosis, trauma, general paresis) associated with chronic alcoholism	4	0
Totals	100	24

Table 1 indicates the final hospital diagnoses in our 124 cases; 85 of these cases were used in the preliminary study previously mentioned. The 39

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§It is our experience that the use of a questionnaire to obtain follow-up information is unsatisfactory. The percentage of returns is low, the information received is often unreliable and misleading, — occasionally quite false, — and not infrequently the former patient resents receiving a questionnaire when, somewhat to our surprise, a visit from a tactful and experienced psychiatric social worker will arouse no antagonism. In a number of cases a carefully worded personal letter to patients living too far away from Boston for visiting elicited the desired information when a questionnaire had brought no response.

others were selected from the alcoholic patients admitted to McLean Hospital during the last five years, and were known personally to one or both of us during their hospital stay.

For the purposes of this presentation the discussion of our material is arranged in the following order: general description of the clinical material including sociologic data, personality traits, psychosexual make-up and drinking habits of the group as a whole; a short discussion of treatment; the results of treatment; conclusions.

General Description of Clinical Material

Sociological Data

The average age of the 100 male patients was forty, with a range from nineteen to seventy-two. From the standpoint of race, American or English blood predominated, being more than four times as common as the next most frequent racial group (Irish); one unexplained fact was the absence of any Jewish patient in the entire group. Protestants were more numerous than Catholics in the ratio of about 4:1. Fifty-three of the patients were married, 30 single, 11 divorced or separated and 6 widowers. Alcoholism had existed in the immediate family of nearly half the patients: this is a significantly higher incidence of alcoholism than is to be found in the families of the non-alcoholic hospital population. Seventeen of the patients came from families where the use of alcohol was known not to have been a problem. The position of the men patients among siblings revealed no evidence that this factor plays a direct or uniform role in predisposition to alcoholic addiction: 8 were only children, 28 the eldest of two or more siblings, 25 the youngest of two or more siblings, while the rest fell in between the extremes of three or more siblings. Among the married patients 52 had children. Thirty-seven of the male patients were college graduates, 42 were high-school graduates, while the others had received less than a high-school education. Forty-nine of the men were classified as business men, 12 in professions, and 24 unemployed (9 of these were retired); the rest were craftsmen, students, laborers and so forth. With regard to physical status, 69 of the patients were classified as having been in good health, 14 in fair and 17 in poor. In the 31 cases where the physical status was abnormal the high incidence of gastrointestinal and neurologic disturbances was noteworthy.

With regard to the sociologic data of the 24 female patients a number of interesting differences and similarities are to be noted as compared to the men: as remarked in our previous paper, the average admission age (forty-three) was significantly higher in the women, the general physical health was poorer and the proportion of college graduates was about a third that of the men, whereas a high-school education was twice as frequent in the non-college women as in the non-college men. The high incidence of familial alcoholism clearly observable in the men was even more striking in the women, being present in every case. There were no single women in the series: 2 were widows, 6 divorced and 16 married.

Personality Traits

In our opinion much doubt is justified as to the psychiatric validity of regarding the human personality as simply a mosaic of character traits — a sort of mysterious and elusive jigsaw puzzle which, when the last pieces have been snugly and neatly tucked into place, presents to the tired but triumphant psychiatrist a clear and composite picture of the individual as a whole. What is here meant by a personality trait is something much more fluid and dynamic: in the course of the careful psychiatric study of each patient, in which an attempt is made to evaluate the current clinical picture in terms of his constitutional endowment and previous experience, there emerge recurring trends, patterns and characteristic modes of adaptive behavior by means of which the individual has attempted again and again to solve his problems and to get along in the world about him and with the other people in it. Are there any such recurring trends or patterns — personality traits — which can be seen, in a fair proportion of the cases, to bear an etiologic relation to the heavy drinking of our alcoholic patients? In so far as we are able to discern the answer is, No. A more variegated collection of personalities and personality types than those of our 124 cases would be difficult to assemble: some were sociable, some seclusive, some stubborn, some easily influenced, some cyclothymic, some schizoid, some intelligent, some dull, and so on *ad infinitum;* the only trait these people seemed to have in common was addiction to the excessive use of alcohol. It is true, as pointed out in our preliminary survey, that many of the men exhibited sociableness and general realistic ability to get along with others, especially at a superficial social level; these traits were striking in 57 patients. Also in 57 patients emotional instability was marked, and definite inferiority feelings were noteworthy in 33. From a careful study of the cases one obtains, however, the impression that these trends reflect secondary developments: that the feelings of inferiority, for example, have in most cases arisen out of situations and circumstances due to the drinking rather

than having been a cause of it. By the time a patient's use of alcohol has become so serious as to necessitate sending him to a mental hospital he has usually been subjected to the several familiar standardized forms of social pressure and sanctions (wife's, parents' and friends' exhortations, threats and so forth) and it is, we believe, these influences, which are secondary to drinking, that are largely responsible for those personality trends which alcoholic patients have been supposed to possess in common. So far as these secondary personality trends are concerned there are no significant differences to be made out between the male and female patients: the absence of inferiority feelings noted among the women of our preliminary study is not borne out in the present series, as in only 5 of the 24 women were such feelings emphasized.

Psychosexual Make-up

In the male patients the sex drive was described as marked in 31 and slight in 19, while only 3 were known to be impotent; the same general percentages held for the women patients. Heterosexual adjustment was considered unsatisfactory in 38 of the men and 15 of the women; overt homosexual tendencies were present in only 9 of the men and in none of the women. In 38 of the men and 17 of the women no homosexual trends, latent or overt, could be made out.

Drinking Habits

There seems to be nothing more difficult to evaluate about a group of alcoholic patients than their drinking habits: the greatest variability obtains from patient to patient and even in the same patient at different times. To attempt to generalize seems fruitless. There are two exceptions: it is usually possible to ascertain fairly accurately when a patient first started to use alcohol, and less accurately when his excessive use of alcohol began to be a problem. The average age when drinking first began in our patients was twenty in the men and twenty-four in the women: on the other hand, heavy drinking began on the average about ten years later in both sexes — at thirty years with the men and at thirty-five with the women. This striking confirmation of the findings in our preliminary study is in accord with our belief that a period of about ten years' drinking is required for the vicious circle of drinking to relieve symptoms caused by previous drinking to become established and for true addictive drinking to set in.

Treatment

Our concept of the principles of the treatment of chronic alcoholism has been developed and expounded in detail elsewhere;[1, 2] here it will suffice merely to recapitulate briefly.

It is our conviction that there are two types or stages of drinking, first, symptomatic drinking, where the alcohol is taken as the result, or for the relief, of the symptoms of some underlying condition, social, mental or physical; and second, addictive drinking — the vicious circle noted above — where the alcohol is taken for the relief of symptoms which have been caused by previous drinking; in a sense, addictive drinking is a later stage or special type of symptomatic drinking where the same agent, alcohol, that has caused symptoms is being utilized for their relief. The treatment of symptomatic drinking is simply the treatment of the underlying pathologic condition, whereas the treatment of addictive drinking is much more complicated: it is first of all essential to break up the vicious circle and bring the patient to attain total abstinence; it is then necessary to deal with the original cause of the earlier symptomatic drinking, which not infrequently has been submerged under years of drunkenness and is often not amenable to direct therapeutic attack. Thus, as a rule the problem becomes one of substituting non-alcoholic and socially acceptable ways of satisfying a patient's needs and of dealing with his problems.

Each of the patients in this study was removed from his accustomed milieu (often under circumstances of the utmost urgency) and, usually against his will, plunged into the atmosphere of a mental hospital with its regular, organized daily routine and, of course, enforced immediate total abstinence. Withdrawal symptoms are treated by non-alcoholic means and all the resources of the hospital in hydrotherapy, physical therapy and so forth are brought into play. In the course of the first week a systematic review of the patient's life is instituted, and as the patient's physical condition improves an attempt is made by psychotherapy and re-education to give him intelligent insight into and understanding of the difficulties that have brought him to a mental hospital, and to equip him for a lifetime of total abstinence by making available resources other than alcohol for dealing with his problems. In 6 men the orthodox psychoanalytic technic of therapy was attempted, although in no case was a complete analysis possible; the periods during which analysis was carried out varied in the several cases from eight weeks to one year. The average duration of hospital stay was one hundred and nine days for the men and sixty-five days for the women.

Results of Treatment

It is possible to divide our 100 alcoholic men and 24 women into three groups depending on the known results of their hospital experiences: first,

a group of 15 men and 4 women who have remained abstinent since their discharge from the hospital (with three exceptions the duration has been at least eighteen months); secondly, a group of 36 men and 8 women who while not remaining totally abstinent have nevertheless shown definite improvement and may be considered to have been benefited by the hospital experience; and, thirdly, a group of 49 men and 12 women whose general behavior, particularly with regard to the use of alcohol, has shown no change for the better subsequent to their treatment.*

It is immediately apparent on perusal of the sociological data, personality characteristics, psychosexual make-up and drinking habits of each of these three groups of patients that no very striking constant differences exist between them which can be considered as having had prognostic value. The average admission age of each group was about the same in the case of the men: forty years for the abstinent group, forty-two for the improved and thirty-nine for the unimproved; whereas with the women the abstinent group was on the average younger than either the improved or unimproved (forty-one years as contrasted with forty-four for each of the latter). None of the other sociological data — marital state, familial alcoholism, sibling position, religion, education and physical status — showed any constant trends which could be correlated with the outcome.

With regard to the personality traits and psychosexual make-up of the three groups the position is about the same, with the exception that the patients who did well seemed on the whole less sociable and tended to be more unstable emotionally — more easily affected by environmental influences — than did those who did poorly. Also the absence of homosexual trends in the abstinent men may be of significance. It is interesting that the abstinent group began their drinking on the average later than the unimproved group: three and a half years later with the men and seven years later with the women, the evident implications being that the earlier in life drinking starts and the longer it has continued the worse the prognosis. The type of drinking — solitary, periodic, continuous or social — seems to bear no relation to outcome, although the trend, previously remarked, for drinking which at first was periodic and social to become, with the passage of time, continuous and solitary is again apparent.

There is the suggestion that patients who have had previous institutional psychiatric treatment elsewhere do not do so well at McLean Hospital as those who have not had such previous treatment. Also, as noted by other investigators[4] the presence of a psychosis, especially delirium, at the time of admission would seem to point in the direction of a more favorable course.

So far as the type of treatment or duration of hospital stay is concerned we are, to our surprise, unable to discern any positive correlation with outcome. The abstinent men had an average hospital residence of one hundred and thirteen days; so did the unimproved group, while for the improved but not cured cases the average duration of hospitalization was one hundred and one days. Similar relations obtained for the women. The 6 men who were exposed to psychoanalytic methods were all unimproved.

It is suggested that the shock many patients experience on finding themselves in a mental hospital is a more potent factor in therapy than one would at first realize; if with this shock come a degree of insight and a realization of the seriousness of their drinking, perhaps one of the most valuable therapeutic contributions the mental hospital has to offer alcoholic patients has been accomplished. This is well shown in one of our female patients who was admitted one day and discharged the next against advice; she was resentful and furious at both her husband and the hospital; yet she has not taken a drink since — almost four years. One wonders if this result could have been improved on had the patient remained a year — or if a prolonged stay might not have tended to remove those very factors which, in her case, seem to have contributed to a favorable outcome. The essential factor here seems to be the clear and dramatic crystallization in the patient's mind of the causal relation between drinking and the critical position in which the patient finds himself (threatened loss of physical or mental integrity). This may be the explanation for the apparent favorable effect of delirium on outcome.

Conclusions

On the basis of the foregoing findings two main conclusions seem justifiable: first, there does not seem to be any one personality pattern or constellation of personality traits which is typically alcoholic — there is no "alcoholic type"; second, the outcome of treatment of chronic alcoholism has little apparent relation to sociological or personality traits, type of therapy or duration of hospital stay.

There are a number of corollaries and subsidiary observations in addition to the foregoing conclusions. In the first place, while there does not seem to be a specific alcoholic type of personality, certain trends — sociability, inferiority feelings and emotional instability — have a high incidence in our group; it is suggested that these traits are secondary to the drinking rather than its cause. Furthermore, the high incidence of alcoholism in

*Eleven of the 124 patients have died since discharge from the hospital.

the families of our alcoholic patients is striking and probably significant. In the second place, there is the suggestion that the period of time during which heavy drinking has existed prior to the beginning of treatment bears a relation to prognosis: the earlier in life drinking starts, the poorer the prognosis.

Our general conclusion therefore is that anyone — normal, neurotic or psychopathic, manic-depressive or schizoid — can become an alcoholic addict if he drinks long enough and heavily enough (on the average about a decade), and that the younger he is when he starts his drinking, the less likelihood there is for his successful treatment in a mental hospital.

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REPORT ON MEDICAL PROGRESS

ORTHOPEDIC SURGERY

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THIS report is in no way intended to cover all that is new in diagnostic measures, clinical entities and methods of treatment; its purpose is to point out those advances that are still in the experimental stage, and to make suggestions which may be productive of a better understanding of orthopedic problems.

Correct diagnosis is the foundation for correct treatment leading to relief of pain, and often to cure of the condition for which the patient seeks advice. It becomes all important, then, that we so conduct our examinations that we can have faith in the conclusions and the diagnosis based on them. In order to accomplish this we must interpret every symptom, every sign, and not be content to go through a routine examination without rationalization.

Pain is probably the most important source of information we have, yet it is one of the most neglected. There are so many types of pain that it is difficult to enumerate them. The chief cause of pain is the tension of structures; as soon as the tension is relieved the pain subsides; a ruptured appendix is a good example. The reaction to a lesion, then, is swelling with tension, causing what is referred to as local pain. Because of the innervation of the structures involved, the brain refers the pain along the peripheral distribution of the nerves of the affected region; this gives rise to so-called "referred pain." This is still primary pain, since it is the direct result of the lesion. So as to protect the region involved, the muscles go into spasm, which is constant and therefore puts the muscles under unusual strain, rendering their attachments sensitive and painful. This type of pain may be referred to as secondary or protective. By analyzing an apparently complex picture of pain in terms of primary and secondary pain, the problem very often becomes simplified, and instead of one's saying that the patient is a neurotic and has pain everywhere, a reasonable explanation may be found.

The above refers particularly to preoperative conditions. Postoperatively we also have various types of pain that should be interpreted and properly evaluated. Any surgical procedure results in local pain, discomfort or soreness; a surgical procedure on the spine or on the extremities necessarily demands a certain period of partial or complete immobilization, with inevitable and sometimes very striking muscle and bone atrophy.

When functional treatment is started there is necessarily a certain amount of protective muscle spasm, with accompanying tenderness over muscle attachments. We also have the discomforts secondary to the mobilization of the joints involved; these are common complaints, usually properly treated. One type of pain often unrecognized is that due to bone atrophy; the atrophy in itself is not painful, but it is accompanied by circulatory stasis aggravated by faulty muscular function. Unless care is taken to relieve this bone congestion by various means, such as elevation and proper exercises, the pain may occasionally be severe enough to interfere with function and a vicious circle is established. Conditions of this type are extremely difficult to treat, and if routine measures are prescribed, results will not be obtained; the treatment must aim to relieve congestion. Interpretation of pain, then, must be our guiding principle in prescribing treatment, and we shall succeed better if we pay more attention to it.

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"Sciatica" is a term which has always been and still is misused; in general it is applied to severe, sometimes disabling pain in the lower extremities. If this term is used it should always be accompanied by an accurate description of the distribution of the pain as pointed out by the patient. The commonest distribution to which this term is applied is that over the posterior aspect of the thigh and posterior and posterolateral calf, and sometimes the lateral border of the foot. This corresponds to the peripheral distribution of the first and second sacral nerves. Until a few years ago it was accounted for on the basis of neuritis, fasciitis and myositis. Then came a period when it was commonly associated with lesions involving the sacroiliac joint. There was good reason for this interpretation, since tuberculosis of this joint is commonly accompanied by this distribution of pain. I am one of those who for years claimed that sacroiliac lesions alone could logically account for it. With the advent of ruptures of the intervertebral disk, another entity accounting for this distribution of pain was added.

The neurologists have as yet not furnished us with a satisfactory explanation of the mechanism productive of this distribution of pain, nor have they told us why lesions of the third, fourth and fifth lumbar intervertebral disks should produce a distribution of pain so very nearly the same. Unquestionably the distribution is only apparently the same, and if we are accurate in recording the patient's statements, we may some day be able to point out variations depending on the particular disk involved. This will never be achieved if we persist in describing pain referred to the lower extremity by the term "sciatica."

Rupture of the intervertebral disk is a distinct clinical entity; about this there can be no argument. It unquestionably accounts for many cases of chronic back pain unsuccessfully treated in the past. On the other hand, many patients suffering from this condition must have been relieved by spinal fusions, even though the real underlying cause was not recognized. The recognition of this lesion has meant definite progress, not only in treating patients presenting it but also in the study of chronic disabling back conditions.

The orthopedic surgeon is no longer going to be content to treat patients with chronic back pain, accompanied by referred pain to the lower extremities, by back braces and plaster casts for any length of time; he is going to institute early neurological examination, accompanied by a lumbar puncture, thereby avoiding delay in recognizing intraspinal conditions. As a matter of fact, the orthopedic surgeon now rarely examines a patient complaining of back pain without testing the reflexes — something which unfortunately was rarely done before the importance of injuries to intervertebral disks was recognized. On the other hand, the neurologist and neurological surgeon would never consider the examination of a patient complaining of pain referred to the lower extremities as complete without performing the test of straight leg-raising. Thus far they have confined themselves to this one orthopedic test, but even so it denotes progress.

It is interesting to note that no satisfactory explanation as to the mechanism of pain production by straight leg-raising has been furnished by either the neurologist or the orthopedic surgeon. Orthopedically the test was supposed to bring about a tightness of the hamstrings, resulting in strain or tension's being transmitted to the sacroiliac ligaments, thereby producing pain. When the pain did not come on until the lumbar spine moved, the test was considered as pointing toward a lumbar lesion. The fact remains, however, that in cases of pain referred to the lower extremity secondary to a lesion of the intervertebral disk, straight leg-raising is productive of pain before the hamstrings become taut and before the lumbar spine moves; at least this is a very common observation. My interpretation of this phenomenon is that raising the lower extremity with the knee straight, particularly if the foot is kept in dorsiflexion, brings about tension of the gastrocnemius and the hamstrings. Since these structures are hypersensitive the tension aggravates the pain. This explanation, however, may not be satisfactory to the neurologist.

Any new clinical entity, any new method of treatment, is apt to be followed by a wave of hyperenthusiasm; as experience is gained the pendulum tends to swing back, and we encounter a period of increasing conservatism. This period has already set in as regards intervertebral disk injuries and their treatment; Lipiodol is no longer used as extensively as it was, since we now recognize that it is not so innocent and inert as at first supposed. Air injections are beginning to take the place of Lipiodol, which is used only when absolutely necessary.

Arthritis cannot properly be referred to as a new clinical entity, but there are certain aspects of the diagnosis and treatment of this condition which have been developed in recent years, and which should be referred to as relatively new and distinctly helpful. The treatment of this condition has gone through cycles of enthusiasm — vaccines, diets of various types, as well as different forms of physiotherapy. At present there is a tendency to adopt a more analytical attitude, evaluating these different types of treatment and possibly favoring

good general hygiene, some special form of therapy if indicated, and attention to the local condition of the joints. The sedimentation rate has proved of distinct value in judging the activity of the disease and the response to various forms of therapy. I believe that this particular test has been effective in evaluating the different specific forms of treatment and thereby has led to the present somewhat conservative attitude.

Hypertrophic arthritis is more commonly referred to as "degenerative joint disease"; this is quite proper, but even this term leaves something to be desired. In the last analysis the condition should be referred to as degenerative joint changes, secondary to wear and tear. It is not a disease process; it is a physiologic process, secondary to advance in age. If we keep this in mind we shall be less apt to subject a patient to elimination of foci of infection which rarely bear any relation to the joint changes; we shall be more apt to look for mechanical reasons for the abnormal wear and tear, and try to eliminate these by correction of mechanics.

A recent development in the surgical treatment of arthritis is encouraging. In the past, arthroplasty by means of an interposed perishable membrane has been successful in a comparatively small percentage of cases. This procedure could never be undertaken during the active stage of rheumatoid arthritis; if it was, it invariably led to failure. The new form of arthroplasty is based on the principle of interposing a permanent mold by which Nature can do her repair work. This mold is made of an inert metal which will not give rise to excessive scar formation and re-ankylosis of the joint. By insertion of such a mold, even during the acute or active stage of the disease, pain is diminished and function improved. The procedure has as yet not stood the test of time; our attitude must therefore be conservative. Surgery of this type should be carried out in selected cases only, and chiefly for the relief of pain, without expecting too great an improvement in function. In cases of degenerative joint disease, particularly when the hip joint is involved, the results are much more encouraging, both as concerns relief of pain and improvement in function.

In relation to the joint, joint changes and joint mechanics, we must keep in mind the innumerable bursae found wherever there is friction on tension. The subdeltoid is the classic example of a bursa apt to give rise to symptoms because of excessive abnormal function of the shoulder. We must not lose sight of bursitis as a frequent cause of local acute pain wherever we have muscles gliding over a bony prominence. Pain over the radial head (tennis elbow), unilateral cervical pain, pain in relation to the superior and inferior angles of the scapula, localized pain in relation to the transverse processes of the lumbar spine, particularly the third, acute pain just above the middle of Poupart's ligament (iliopectineal bursitis), pain over the greater femoral trochanter and pain in numberless other regions can very often be accounted for on the basis of bursitis. Injection of normal saline under novocain anesthesia is very effective in the treatment of bursitis and is gradually taking the place of open surgery, even when the x-ray film shows calcium deposits.

The treatment of osteomyelitis is entering a new phase in so far as more attention is being paid to its bacteriological aspect; the patient's general physical condition is considered first, surgical treatment and local condition second. Before the patient is subjected to surgical treatment the possibility of chemotherapy is duly weighed. Because of the increasing importance of the bacteriological aspect, we find here and there surgeons who have gained a wide knowledge of bacteriology and are therefore qualified to deal with the surgery of septic conditions. This is distinct progress, and will lead to infinitely better understanding of the conditions underlying osteomyelitis.

There is an increasing demand for the services of the orthopedic surgeon in the treatment of fractures. This is natural, since his specialty brings him into constant contact with joint function and the problems involved. After all, the treatment of fractures depends on a knowledge of the neighboring joints which the general surgeon cannot be expected to possess. Consequently, it seems fair to say a word about the progress in the treatment of two fractures, — those of the spine and of the neck of the femur, — progress for which orthopedic surgeons have been responsible.

Fractures of the spine until recent years were left without correction; this commonly gave rise to faulty joint function, with resulting partial or complete disability. The correction of fractures of the vertebral bodies has returned a large number of these patients to their pre-injury occupations.

Fracture of the neck of the femur has always been a difficult problem, and consequently has been referred to as "the unsolved fracture." Internal fixation of this fracture has led to a saving of many lives, eliminated much of the pain and achieved bony union with good function in as high a percentage of cases as in fractures into other joints.

The increasing tendency in the treatment of congenital deformities is to guide growth gradually rather than to correct deformities immediately. This is logical treatment, since immediate correction by open surgery commonly leads to inter-

ference with growth, thus causing secondary deformities.

Opinion as to the treatment of tuberculosis of bones and joints is still divided. It is fair to say that surgical treatment is gaining in favor, since it provides the patient with a permanent internal protection against recurrence. If surgical treatment is undertaken during the period of growth, this should never be done until the patient is in the optimum physical condition, and surgery should be performed in such a way as to cause the minimum interference with growth. The arguments of those who favor conservative non-operative treatment are based on less interference with growth, less chance of secondary foci; scientific support of the arguments is lacking.

No startling discoveries in the treatment of poliomyelitis have been made in recent years. Excellent advice on the treatment of the acute stage can be found in current articles. Treatment during the later stages consists in correction of deformities which have developed in spite of good treatment or because of faulty treatment; such measures consist chiefly in arthrodesis of joints. Muscle transplantation, which may be referred to as treatment aiming to compensate for paralysis, is becoming simplified and therefore increasingly efficient.

264 Beacon Street.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25451

PRESENTATION OF CASE

A forty-two-year-old ex-sailor, ex-soldier, ex-prize-fighter and salesman was admitted to the hospital complaining of jaundice of about five weeks' duration.

Eighteen years before admission the patient developed a chancre and a year later suffered from iritis. He then consulted a physician who diagnosed syphilis. Over the following ten-year period he received at least forty-eight injections of neoarsphenamine or sulfarsphenamine, twenty injections of tryparsamide and one hundred and five of bismuth. Potassium iodide and mercury were taken by mouth. For the seven-year period prior to admission he received no antisyphilitic therapy. Three lumbar punctures performed thirteen, twelve and eleven years before entry gave spinal-fluid total proteins ranging from 59 to 66 mg. per 100 cc. and negative Wassermann tests. However, blood Hinton tests were persistently positive and Wassermann tests occasionally negative. These data were obtained from the patient's outpatient records, which also showed that no central nervous symptoms had ever been elicited. About four and a half months before entry he noticed marked anorexia and that his urine was becoming increasingly brown. Approximately five weeks before entry his eyes became yellow. He had had no weight loss, nausea or vomiting, nor had he noticed any clay-colored or tarry stools.

For many years he had drunk from one to two pints of hard liquor a day and his eyes had been intermittently "yellow" for fifteen years before admission. For a long while the patient had had crusting in the nasal passages, with bleeding when he forcefully blew his nose. His family history was not contributory.

The physical examination revealed a well-developed and well-nourished, flushed, icteric, nervous man, who did not appear acutely ill. His speech was slow, and there was a tremor of the hands and jaw. The nasal mucous membranes were atrophic and crusted, the tongue tremulous. Examination of the lungs was normal. The heart was not enlarged. There was a loud short systolic murmur heard in the second left intercostal space and transmitted well into the great vessels of the right neck. The blood pressure was 144 systolic, 80 diastolic. The liver was percussed at the level of the fifth rib anteriorly and was felt as a mass without gross nodularity two fingerbreadths below the costal margin. The spleen was palpated two to three fingerbreadths below the costal margin. There was slight shifting abdominal dullness. Examination of the rectum revealed internal hemorrhoids. Slight pitting edema was noted around the ankles.

The temperature was 101°F., the pulse 90, and the respirations 22.

Examinations of the urine showed specific gravities ranging from 1.010 to 1.022, albumin from 0 to ++ and no sugar; bile varied from 0 to +; the sediments contained innumerable red cells, and the white cells varied from 10 to "many" per high-power field; there were no casts. The blood examinations revealed red counts from 2,600,000 to 3,500,000 with 60 per cent hemoglobin, and white-cell counts from 4700 to 5400 with 66 per cent polymorphonuclears. The stools were brown and guaiac negative. The blood Hinton test was positive and the Wassermann weakly positive. The serum protein was 6.4 to 7.4 gm. per 100 cc., the van den Bergh 3.9 mg. A bromsulfalein liver test showed 45 per cent dye retention. The Takata-Ara test was strongly positive, and the formol-gel test positive after forty-eight hours. A lumbar puncture revealed normal dynamics with a slightly icteric fluid which had a total protein of 30 mg. per 100 cc. The spinal-fluid Wassermann test was negative. The gold-sol curve read 0012210000. Abdominal paracenteses yielded 1600 and 3000 cc. of clear yellow transudate, which showed no tumor cells.

X-ray studies of the esophagus revealed extensive varices. A chest plate showed the diaphragms in a high position, with the heart slightly enlarged but without characteristic configuration. The lung fields were clear.

The patient ran a slow but steady downhill course. He spiked a daily temperature up to 103°F. The pulse varied between 80 and 120. He was treated intensively with potassium iodide, vitamins, transfusions and a high-carbohydrate diet. However, he progressively became more jaundiced, mentally dull and confused. On two occasions he vomited several ounces of blood. He died on the twenty-ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. CHARLES L. SHORT: Will you show the films, Dr. Holmes?

DR. GEORGE W. HOLMES: One of the charac-

teristics of esophageal varices is that they are not present in all films at all times. For instance of these three films on the screen the first and third are suggestive but not definitely characteristic, whereas the findings in the middle film justify a positive statement that varices are present. The heart shows surprisingly little — certainly no evidence of disease of the great vessels. It is questionable whether there is any disease of the heart at all.

DR. SHORT: Have there been any exceptions to the rule that if you find varices you can make a diagnosis of portal obstruction — excluding this case of course?

DR. HOLMES: Dr. Schatzki has reported one or two cases of congenital anomalies. We had one case where a picture indistinguishable from varices was produced by something entirely different. However, I think that in the majority of cases this picture means portal obstruction.

DR. SHORT: Would you be willing to predict how long the portal obstruction has been present from the extent of the varices, or is that impossible?

DR. HOLMES: It is impossible.

DR. SHORT: In view not only of the varices but also of the other findings, I think we can accept as a fact that this patient had liver disease with portal obstruction. There was jaundice, an enlarged liver and spleen, ascites, evidence of impaired liver function and, finally and probably of most importance, demonstration of the varices. I think we can also assume that the patient died of liver insufficiency. The fever can be explained on that basis, and we have no evidence of any intercurrent infection. The rather loud systolic murmur could be accounted for by his anemia, and with the negative chest x-ray film I do not believe we have to make a diagnosis of heart disease. The anemia with a rather low white-cell count is quite characteristically found in disease of the liver. We do not have to assume that he had had hemorrhages.

The only point in the story that is difficult to bring in is the constant finding of large quantities of red cells in the urine, along with some white cells. That tends to make you think of some complicating condition, — possibly bacterial endocarditis with renal infarcts, — but again there is no positive evidence, and we shall either have to call the hematuria an unimportant coincidental finding or pin it on the hemorrhagic tendency which is present in liver disease. Evidently the service accepted it this way because no further investigations were carried out, unless perhaps they were not done because the patient was too sick.

I shall assume then that this patient died of liver insufficiency alone. Next, the more difficult question comes up as to what was the cause or the causes of the liver disease. He had, as you remember, a large amount of antisyphilitic treatment including arsphenamine, which is most important in causing liver damage. He evidently was observed in the Out Patient Department, and there is no history of his having had jaundice while under treatment with arsphenamine. It is possible that he had subclinical latent damage to the liver developing in the course of the treatment, but that is impossible to prove, and the fact that he had had a ten-year interval without any antisyphilitic treatment vitiates the possibility that antisyphilitic drugs played a role. Next, we have to try to find out what part syphilis played in this case. Of course, syphilis may be a factor in any type of liver disease; on the other hand, at autopsy any patient with syphilis may show scars in his liver and have had no symptoms during life. Then there are cases reported of typical portal cirrhosis which were apparently due to syphilis. But that is a rather rare condition, and very difficult to prove, I believe, during the patient's life. Even if the therapeutic test fails, I do not believe we can rule out syphilis as a possible cause of portal cirrhosis in a patient with this disease. But in view of the comparative rarity of this condition, and the fact that he was quite adequately treated for syphilis, I shall dismiss the possibility of syphilis as a cause for the acute liver damage, although I think it is not improbable that some scars may be found by Dr. Mallory in the liver, representing healed gummas.

We are left then with the ordinary type of portal cirrhosis, in which we know alcohol is a factor. We cannot say from the varices that the process was of long standing, but it may well have been so in an asymptomatic form. The only symptoms he had until five months before admission were occasional yellowing of the eyes and nosebleeds, and neither of them may have been really significant. I think it is more logical to believe that he had a portal cirrhosis of long standing and that he died with what is called an acutely decompensated liver. The question is whether the final episode was of the nature of an acute necrosis of the liver or simply an exacerbation of the portal cirrhosis. He had a rather low van den Bergh test and only a moderately impaired liver function when he came in, but of course he was not acutely ill at that time. We do not know what the tests showed later on, but from the picture here and from the duration of the terminal course, I should say that simple portal cirrhosis with an exacerbation could account for his death without bringing in acute liver necrosis. So I should expect to find

at autopsy a long-standing fibrotic process resembling portal cirrhosis, and perhaps some evidence of activity of this disease in the liver cells.

In any case of liver disease with a rapid, downhill course we have to think of two possible complications. One is the development of a primary hepatoma of the liver. There is no positive evidence of that in the form either of a palpable tumor or of one demonstrable by x-ray. There is no evidence of metastases, so I do not believe we can make that diagnosis although we always have to keep it in mind. The second possibility is portal thrombosis shortly before death. Again, we cannot prove that, and the diagnosis is not often made in life. He apparently did not have a sudden increase in ascites, so we shall have to say there is no proof that he had portal thrombosis.

In conclusion I think this patient died in an acute exacerbation of an alcoholic or portal cirrhosis, with a liver that may show some scars of old gummas.

DR. TRACY B. MALLORY: Are there any other suggestions?

DR. WILLIAM B. BREED: I should like to ask Dr. Holmes, in view of what Dr. Short suggested about hepatoma, whether that angle in the right diaphragm means any more to him.

DR. HOLMES: No; I think it is well within normal limits for his build.

DR. PAUL S. HANSEN: When he was on the wards he had a positive Wassermann test and had had negative tests in the past. We wondered if that indicated active visceral syphilis. As for the hematuria we did not ignore it. He had a negative intravenous pyelogram, and we wondered whether the hematuria might represent a defect in the blood-clotting mechanism or possibly a varix in the kidney. We could not explain a varix anatomically but thought there might be an associated thrombosis or partial occlusion of the renal vein.

DR. MALLORY: I remember having been asked to see this patient on the ward with regard to the question as to whether syphilis played any part in his liver disease. I was particularly impressed by an almost lyrical description which he gave me of an *estaminet* just back of the lines in France in 1918 which specialized on Demerara rum, so I think he was already a chronic alcoholic even during the last war, when he was a fairly young man. At that time I expressed the opinion that syphilis would be found to have nothing to do with his hepatic insufficiency, and I am still of that opinion after the autopsy.

CLINICAL DIAGNOSES

Cirrhosis of liver (? portal, ? luetic).
Acute hepatitis.
Esophageal varices.
Serological lues.

DR. SHORT'S DIAGNOSES

Portal (alcoholic) cirrhosis, decompensated.
Healed gummas of the liver?

ANATOMICAL DIAGNOSES

Cirrhosis of liver, alcoholic.
Esophageal varices.
Jaundice.
Ascites.
Bronchopneumonia, localized, right upper lobe.
Perisplenitis.
Pulmonary tuberculosis, left apex, healed, fibrous.
Operative scars: herniorrhaphy, right; abdominal paracentesis.
Hemorrhage into gastrointestinal tract.

PATHOLOGICAL DISCUSSION

DR. MALLORY: He had what we pathologists always call a hobnail liver. I formerly had the impression that that was a very descriptive term, but after trying it out for several years on medical students I began to wonder about it. Apparently present-day medical students have never seen hobnails. I asked what size hobnails are and got answers varying from 1 up to 35 mm. in diameter.

This particular liver showed very uniform nodules varying from 2 to 3 mm. in diameter. It was still a little larger than normal, weighing 1800 gm. We know that patients with alcoholic cirrhosis go through a stage in which the liver is greatly enlarged — sometimes up to 4000 or 5000 gm. This had shrunk considerably from that stage but was still at the upper limit of normal. The esophageal varices were very extensive, and there was no doubt about them anatomically. The spleen, as you would expect with portal obstruction, was considerably enlarged, weighing 600 gm., and showed early stages of the characteristic fibrotic changes that you get with long-standing portal obstruction. It is worth emphasizing that during life the leukopenia which is characteristically found with chronic portal obstruction was present. I am strongly of the opinion that this finding is due to passive congestion of the spleen, because it disappears with splenectomy: whether or not the patient has cirrhosis makes no difference. Following splenectomy the

white count will run around 10,000 as long as the patient lives. We found nothing to account for the hematuria. Our only guess is that it must have been a manifestation of a purpuric tendency. There were red cells found in the convoluted tubules, but there was no significant glomerular damage to account for it.

DR. SHORT: Was there any evidence of activity in the liver cells?

DR. MALLORY: There was no significant evidence of recent degeneration. I should have to assume it was just a liver that had been running along on a low reserve and suddenly became decompensated. There was no anatomical evidence of syphilis even despite a complete examination of the central nervous system.

CASE 25452

PRESENTATION OF CASE

A fifty-two-year-old, white married woolen-mill foreman was admitted complaining of weakness following a massive hemorrhage by rectum and fainting two weeks before entry.

About four and a half months before admission the patient noted a gradual onset of gastrointestinal disturbances with alternating constipation and mild diarrhea. For a month laxatives gave moderate relief. He began to lose weight, became anorexic and weak and suffered "indigestion," with variable amounts of gaseous distention. A number of bad teeth were pulled about three weeks before entry. Several days later he had a sudden massive hemorrhage by rectum, consisting of large amounts of bright-red blood, and subsequently passed black stools. He was brought to an outside hospital in shock. The systolic blood pressure was 50. In the hospital he continued to show traces of blood in the stools for several days. After this had ceased and a number of transfusions had been given, a barium enema was done, which showed a large dilated rectum and a slowly filling colon. There was an irregular area in the sigmoid suggestive of carcinoma. His anemia responded well to the transfusions, but he remained toxic and ran a septic type of temperature for several days. The red-blood-cell count was 3,150,000 two days before entry, and the patient felt much better. He was then brought to this hospital for further treatment.

His past and family histories were noncontributory.

Physical examination showed a pale man who evidently had lost weight. He had no teeth. His pharynx was somewhat injected. No peripheral lymph nodes were noted. Examination of the lungs was negative. The heart was negative. The blood pressure was 98 systolic, 60 diastolic. The abdomen was soft and slightly distended. Peristalsis was active, and there was no tenderness or spasm. In the epigastrium there was a questionable mass, possibly the left lobe of the liver. The extremities were negative. A neurological examination was negative.

The temperature was 99°F., the pulse 82, and the respirations 20.

Examination of the urine was negative. The blood showed a red-cell count of 3,980,000 with a hemoglobin of 65 per cent, and a white-cell count of 5400 with 75 per cent polymorphonuclears. The nonprotein nitrogen of the serum was 20 mg. per 100 cc., and the protein 5.1 gm.; the chlorides were equivalent to 92 cc. of N/10 sodium chloride. A blood Hinton test was negative.

X-ray films of the chest revealed multiple discrete areas of soft hazy density scattered throughout both lung fields. The hilus shadows were a little prominent on both sides and slightly lobulated. A barium enema passed without interruption to the cecum, and no constant defects were demonstrated. Two days later this was repeated. The colon was empty and well visualized. It showed no defects, and the terminal ileum was not remarkable. A gastrointestinal series showed the stomach to be elongated and displaced to the left, though it showed no defects. The first portion of the duodenum filled readily and showed pressure defects on its superior margin; there was a similar rounded defect on the superior margin of the second portion. At six hours the stomach was empty and the motor meal lay in the terminal ileum and proximal colon. The hepatic flexure was displaced downward and medially. There was no evidence of intrinsic disease in the upper gastrointestinal tract, but there was evidence of marked enlargement of the liver.

On the thirteenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD L. YOUNG: The history of this case certainly gives us little to go on. There had been only four months of rather vague intestinal symptoms which do not point to any specific portion of the gastrointestinal tract, and there was one massive hemorrhage which might have come from any point from the esophagus downward. We inevitably turn for help to the radiologist and we read of a suggestion of something that displaced the stomach and the hepatic flexure and slightly deformed the duodenum, apparently by external pressure. Dr. Hampton, can you help us out before we begin to do what guessing we can?

DR. AUBREY O. HAMPTON: We found no varices

or enlargement of the spleen, but fairly definite evidence of enlargement of the liver. I think the pressure defects in the duodenum represent pressure from the liver or gall bladder. The first one described is at the beginning of the second portion of the duodenum. That might be attributed either to gall bladder or liver. It is in the area of each. The examination of the colon in the hospital appeared normal, but on this film at another examination there was something that suggested spasm or certainly a transitory defect in the sigmoid. We have seen such spasm with diverticulitis and extrinsic cancer. It is not the picture of intrinsic disease. On the chest plate there are definite round nodules scattered through the lung. I say "definite," though they are not easily seen at first glance; they are there, nevertheless, and they average about 1 cm. in diameter. There also are irregular dense lines running toward the lung root on the right side.

Dr. Chester M. Jones: Is that picture enough to make you fairly certain they are metastases, or does it only make you suspicious?

Dr. Hampton: I think we should be quite certain.

Dr. Young: Is it true that a posterior-wall ulcer of the duodenum or esophageal varices might be missed in x-ray examination?

Dr. Hampton: Yes. We have missed both of them.

Dr. Young: In spite of my question to Dr. Hampton, the whole picture seems to be against esophageal varices and posterior-wall ulcer although either might produce hemorrhage. Even a very acute gastritis has been reported as the cause of massive hemorrhage. The other conditions that cause bleeding so seldom cause a massive hemorrhage of this type that I think we can throw them out. There were black stools so that almost certainly the hemorrhage came from a lesion higher than the one first suspected, that is, a sigmoidal carcinoma. It would seem to me that the evidence points toward the upper gastrointestinal tract. The slight temperature, the loss of weight, the evidence of scattered pulmonary lesions by x-ray make cancer the most probable diagnosis and the lesion must have involved the gastrointestinal tract. The only way in which I can fit all the facts together is to make a diagnosis of retroperitoneal malignant tumor that has involved the bowel. I am reminded of a case that I saw at autopsy here some time ago, one of retroperitoneal sarcoma that had ulcerated through the duodenum and resulted in a massive hemorrhage which was the cause of death. I do not know where else to place the primary lesion. Of course this pressure defect and the fact that this epigastric mass felt like the liver make me wonder if there are actually an atypical type of portal obstruction and portal cirrhosis with esophageal varices, but I am going to put that far down the line and make cancer outside the gastrointestinal tract and ulcerating into it as my first bet.

Dr. William B. Breed: On the evidence of the record, what were the indications for exploration in this case?

Dr. Young: The fact that nobody knew what was the matter and the wild chance that something might be discovered that would help him. In answer to the question as to whether he advised operation following a diagnosis of cancer of the head of the pancreas, Dr. Fred Shattuck used to say: "Yes, because of the fallibility of human diagnosis." I think there may have been some condition present which could have been helped surgically, and in any case I should have operated to establish a diagnosis because if it were retroperitoneal lymphoma a considerable degree of relief might be obtained with radiation therapy.

Dr. Breed: I was wondering whether one could accept the x-ray evidence of metastases to the lungs. That might influence you somewhat in exploration.

Dr. Young: I practically forced Dr. Hampton to say "yes."

Dr. Hampton: I went on probabilities, about nine out of ten.

Dr. Breed: Would the presence or absence of neoplastic nodules in the lungs make any difference in your decision to operate?

Dr. Young: If I were sure the lungs were filled with carcinoma, of course I should not operate.

Dr. J. H. Means: The thing that bothers me is that I cannot find any record of the rectal examination, but I suppose it was done. I do not believe that disease in the rectum has been ruled out, even though it is a little strange to have a massive hemorrhage from a rectal cancer.

Dr. Young: Did you ever see one give tarry stools?

Dr. Means: They may be black from some other reason. I think he should have had a rectal examination.

Dr. Marshall K. Bartlett: Both rectal examination and proctoscopy were done, and both were negative.

Dr. Young: I have never seen a carcinoma of the large bowel that resulted in tarry stools or a massive, nearly fatal hemorrhage.

Dr. Means: Nor have I.

Dr. Leland S. McKittrick: I have seen a carcinoma of the rectum that gave massive hemor-

rhage, the blood going up as well as down, and then the patient had dark stools afterward. Furthermore, I have seen patients explored for massive hemorrhage and nothing found.

DR. TRACY B. MALLORY: Do you wish to tell the operative findings, Dr. Bartlett?

DR. BARTLETT: The colon was entirely normal, also the stomach and duodenum. About two thirds of the way down the small bowel was a segment about 60 cm. in length that was abnormal. In this segment multiple areas of thickening of the wall 1 or 2 cm. in width were found which tended to encircle the lumen of the bowel. The thickenings were soft and did not feel like carcinoma. About 180 cm. of small bowel was resected.

DR. MALLORY: What was your preoperative diagnosis?

DR. BARTLETT: I believe we guessed carcinoma of the gall bladder, but we certainly were not very sure about it.

CLINICAL DIAGNOSIS

Carcinoma at head of pancreas or of gall bladder.

DR. YOUNG'S DIAGNOSIS

Retroperitoneal malignancy involving the small intestine.

ANATOMICAL DIAGNOSES

Lymphoblastoma, Hodgkin's type, with involvement of ileum, lung, liver, spleen, adrenals and thyroid.
Septicemia (*Bacillus coli*).
Pulmonary infarct, left lower lobe.
Hydrothorax, serosanguineous, bilateral.
Pulmonary edema, marked.
Operative wound: resection of segment of ileum.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The lesions of the small intestine proved to be shallow ulcers with slightly indurated margins. It was quite obvious that they represented malignant tumor, but it was not too evident what the type was. Fortunately, however, a biopsy was taken of a metastatic nodule of the liver and on that it was perfectly clear that we were dealing with Hodgkin's disease. The patient died rather suddenly a few days after operation and came to autopsy. We found many Hodgkin's nodules throughout the liver and a few in the spleen, with considerable involvement of the retroperitoneal nodes and multiple lesions throughout the lungs. There was a terminal pulmonary embolus which was at least in part, if not wholly, responsible for his death. If this patient had survived the operation and then had x-ray treatment, it is quite likely his life might have been prolonged for some time.

DR. MCKITTRICK: Is it common for Hodgkin's disease to give discrete nodules within the lung such as this man had?

DR. MALLORY: It is not particularly common but does occur. That is the one form of lymphoma that does involve the lung with significant frequency. Hodgkin's disease can on occasion simulate tuberculosis of the lungs in every respect or look, as this case did, like metastatic cancer.

DR. MEANS: If you took a series of cases of cancer of the small bowel, have you any idea what percentage would be due to lymphoma?

DR. MALLORY: I rather think over half.

DR. JONES: Was the liver as large as it seems to be on the x-ray plate?

DR. MALLORY: It weighed 2100 gm., which is large but not tremendously so.

DR. JONES: Would that account for the pressure defects in the duodenum?

DR. HAMPTON: I think that they were probably due to gall bladder.

DR. MALLORY: Dr. Hampton, if you had been asked to look specifically for a lesion in the small bowel, would you have found it?

DR. HAMPTON: I doubt it. These lesions are hard enough to find in the stomach, and if there is not a large mass of ulcerative tumor, we usually miss it.

DR. MEANS: What was the actual source of the blood?

DR. MALLORY: It was not determined in this case. In the majority of stomach cases with massive hemorrhage one can find erosion of a major vessel. We have not had much luck finding the source of hemorrhage with tumors lower down — below the duodenum, I should say.

DR. JONES: There was one curious laboratory finding of interest. After a good deal of bleeding the patient had a white-cell count of 5400. That is unusual and suggests the possibility of intrahepatic disease. It is characteristic of primary liver disease, and I think that Dr. Frank Hunter has told me of cases with just this picture that had a good deal of diffuse infiltration of the liver with lymphomatous tissue.

DR. MALLORY: We made a number of sections of the bone marrow, thinking the blood picture could be explained on bone-marrow metastases. We found no evidence of Hodgkin's disease, but there was a marked hyperplasia of red cells and marked aplasia of white cells, a picture almost suggesting mild agranulocytosis.

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BLUE CROSS BENEFITS

A letter published in this issue of the *Journal* calls attention to the changes in benefits provided by the Associated Hospital Service Corporation of Massachusetts that have been necessitated in order to ensure future stability of the organization and, hence, to protect the interests of all participants. Chief blame for these changes is placed on abuses practiced by both subscribers and physicians. Most of these have been apparently due to a misunderstanding in regard to just what is provided by a Blue Cross membership. This is being cleared up, and recent figures show that the great majority of subscribers and physicians, particularly the latter, are adjusting themselves to the letter and spirit of the contracts as soon as they thoroughly understand them. An example of this is the distinct cutting down on the part of physicians in sending subscribers to hospitals under non-emergency conditions for diagnostic purposes or periodic health examinations, neither of which is included in the contract.

An appreciable number of patients are still remaining extra days in hospitals at the expense of the Blue Cross. In some cases this has occurred after the physicians have said that the patients could be discharged, and in other cases the physicians, because the Blue Cross was paying the bills, have not encouraged the patients to leave the hospital as soon as they would those patients who were paying their own way. The subscriber's contract is so arranged that if the subscriber stays in the hospital after the physician recommends discharge the bill is supposed to be borne by the patient.

It seems only reasonable that subscribers should abide by the terms of their contracts and that physicians should treat Blue Cross members in the same way that they treat other patients. In this way an unfair financial burden will not be placed on the Blue Cross and any additional reductions in benefits will probably be avoided.

A NEW OPERATION FOR TRIGEMINAL NEURALGIA

Neuralgia of the face of a paroxysmal and severe type has been known from the very earliest times of medicine. A precise description of this disease was not given, however, until 1776, by John Fothergill. As medicinal treatment failed, trigeminal neuralgia was one of the first neurological conditions to be attacked by the surgeon. At first the peripheral nerves were evulsed, only to find that they grew back promptly and the pain returned within a few weeks or months. Next the gasserian ganglion itself was excised, a marked step in progress, for this removed the pain permanently and, for the first time, relief was given for one of the most serious diseases in medicine. In the days before the gasserian ganglion operation many patients were known to have committed suicide rather than tolerate the repeated attacks of pain. The next most important step in the history of the treatment of this disease was the operation of posterior root resection, devised by Spiller

and Frazier, neurologist and surgeon, respectively, of Philadelphia. Following the Spiller-Frazier operation, many modifications of the original technic were developed by other investigators. The motor root, which passes along with the posterior sensory root, was usually avoided. In place of the approach to the posterior root under the temporal lobe Dandy, in 1925, developed a technic of exposing the root through the cerebellar approach and by partial resection succeeded in saving the upper branch in cases in which that was not involved, thus preventing the keratitis which often followed the excision of the entire root.

None of these operations, however, although they relieved pain, were entirely satisfactory. The patient was always left with anesthesia of the side of the face, often extremely annoying, particularly in eating, when food collected at the corners of the mouth and was unnoticed by the individual. Secondly, there was always the possibility of infection of the eye, due to the absence of the normal wink reflex, the sensory component of the reflex being abolished. Thirdly, there was a group of cases in which, in spite of total resection of the posterior root, pain of another form persisted in the side of the face. In spite of these defects, patients were extremely grateful for the relief from pain afforded by this operation and many thousands of patients have been helped in the past.

The next step was to devise some operation which would stop the pain, but, at the same time, preserve sensation in the side of the face. This has now been accomplished by Dr. Olof Sjöqvist,* working in the Neurosurgical Clinic of the Serafimer Hospital in Stockholm. There, under the instruction of Dr. Olivecrona and Professor Häggqvist, Sjöqvist was able to work out the pathway of the pain fibers as they passed through the posterior root and into the medulla. These fibers were first isolated by the ingenious method of carefully measuring the size of the fibers, knowing, as had been previously discovered, that pain fibers are much smaller in diameter than those carrying other forms of sensation. Thus, by counting and measuring the number of fibers in a given section, he was able to show that the pain fibers were carried in a special tract. It is this tract which is now being attacked surgically by making a section of it as it passes through the medulla, in an attempt to obliterate completely the pain pathway. The operation has been done with some success on nine cases, as reported by Sjöqvist. The results, however, have not all been favorable and there are complications which may seriously mitigate against the wide use of this surgical procedure. It is still too early to place the operation in the hands of general surgeons, for only further experience by trained neurosurgeons will enable us to judge of its eventual value in conquering one of the most intractable diseases in all medicine.

*Sjöqvist, Olof: *Studies on Pain Conduction in the Trigeminal Nerve*, 139 pp. Helsingfors: Mercators Tryckeri, 1938. The conduction of pain in the fifth nerve and its bearing on the treatment of trigeminal neuralgia. Yale J. Biol. & Med. 11:593-600, 1939.

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Boston

SEPSIS FOLLOWING FORCEPS DELIVERY

Mrs. M. M., a twenty-six-year-old primipara, was admitted to the hospital January 26, 1912, in active labor of six hours' duration. She was at term.

The family history was negative. The patient had never had any serious illnesses or operations. Catamenia had begun at twelve and were regular with a twenty-eight-day cycle. The last normal period began April 12, 1911, making the expected date of confinement, January 17.

Examination at entry revealed a normal primipara in active labor. The heart was not enlarged, the rate was regular, and there were no murmurs. The blood pressure was 115 systolic. The external pelvic measurements were normal. The baby was presenting by the vertex in the OLA position. The fetal heart rate was 150 and was best heard in the left lower quadrant. The mother's temperature was 98°F., and the pulse 88.

Sixteen hours after the onset of labor the membranes ruptured spontaneously. Examination revealed the cervix half dilated with an edematous anterior lip. The head was low. Three hours later the patient was fully dilated except for a

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

persistent edematous anterior cervical lip. The patient was anesthetized and prepared for delivery. Forceps were applied and moderate traction brought the baby's head down on to the perineum. The blades were then removed and the head delivered. There was only a slight tear of the mucous membrane on the left side of the vagina. The placenta was delivered with a great deal of difficulty by the Credé method but finally came away intact. There was considerable bleeding following the birth of the placenta. A hot intrauterine douche was therefore administered, followed by alcohol.

The morning following delivery the temperature was 98°F. At 1 p. m. it was 101.2°F. The pulse went to 120. The patient complained of tenderness in both lower quadrants. There was some voluntary spasm in the lower abdomen, and slight distention. The patient seemed quite ill. Another intrauterine douche was administered, and ice caps were applied to both lower quadrants. Fluids were forced by mouth, and she was given 30 cc. of whisky every hour.

During the course of the next three days the temperature and pulse gradually returned to a normal level. On the tenth postpartum day the patient had a chill and the temperature rose to 103.4°F. The cervix was dilated, and some pus was evacuated from the uterus. Intrauterine douches of sterile water and alcohol were given. At this time the patient still complained of lower abdominal tenderness, which was worse on the left.

During the next week the patient ran a spiking temperature up to 105°F. The pulse ranged around 120. On February 12, seventeen days after delivery, she passed a tapeworm. For some unexplained reason her temperature then became normal, and she was discharged four days later. A discharge examination revealed a soft, nontender abdomen, moderate rectocele, slight cystocele and a good perineal body; the uterus was retroverted and drawn to the left, and there was considerable induration in the left vault.

Comment. This case occurred in 1912 and is typical of the treatment in vogue at that time. The patient was one of a series of septic cases that occurred during a hospital epidemic. Today it is barely possible that the use of pituitrin and intelligent fundal pressure might have done away with the need of the forceps operation. Certainly today the intrauterine douche which was used to control bleeding and the intrauterine douches followed by alcohol which were used during the febrile course of the convalescence would not have been employed. It might be said that this patient got along well in spite of the intrauterine douche, not because of it, for certainly no greater contraindication could exist than the physical findings described in this case. Low abdominal pain and spasm suggested beyond question the possibility of tubal involvement and the final examination which demonstrated "considerable induration in the left vault" bears out the assumption that the infection had spread beyond the uterus. Today the treatment would have been entirely conservative. Uterine and blood cultures would have been obtained, chemotherapy would have been instituted if the cultures had so indicated, ice would not have been applied to the abdomen, and the uterus would have been left entirely alone.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions of the Medical Postgraduate Extension Courses have been arranged for the week beginning November 13:

BARNSTABLE

Sunday, November 19, at 4:00 p.m., at the Cape Cod Hospital, Hyannis. Common Problems of Neurology: Indications for lumbar puncture. Instructor: H. Houston Merritt. Donald E. Higgins, *Chairman.*

BRISTOL NORTH

Thursday, November 16, at 4:00 p.m., at the Morton Hospital, Taunton. Convulsions in Infants and Children — Etiology and Treatment. Instructor: Louis K. Diamond. Lester E. Butler, *Chairman.*

BRISTOL SOUTH (New Bedford Section)

Friday, November 17, at 4:00 p.m., at St. Luke's Hospital, New Bedford. Head and Spine Injuries. Instructor: Donald Munro. Robert H. Goodwin, *Chairman.*

ESSEX NORTH

Friday, November 17, at 4:30 p.m., at the Lawrence General Hospital, Lawrence. Indications for Cesarean Section. Instructor: Thomas R. Goethals. John Parr, *Chairman.*

ESSEX SOUTH

Tuesday, November 14, at 4:00 p.m., in the Conference Room of the Salem Hospital, Salem. Syphilis in Pregnancy and the Offspring. Instructor: Francis M. Thurmon. J. Robert Shaughnessy, *Chairman.*

MIDDLESEX EAST

Tuesday, November 14, at 4.00 p.m., at the Melrose Hospital, Melrose. Cardiovascular Disease: Eleven important questions about heart disease and their answers. Instructor: Paul D. White. Walter H. Flanders, *Chairman.*

MIDDLESEX NORTH

Friday, November 17, at 4:45 p.m., at St. John's Hospital, Lowell. Gonorrhea in the Female. Instructor: Sylvester B. Kelley. William S. Lawler, *Chairman.*

WORCESTER (Milford Section)

Tuesday, November 14, at 8:30 p.m., in the Nurses' Home of the Milford Hospital, Milford. Complications in Obstetrics Illustrated by Case Histories. Instructor: M. V. Kappius. Joseph Ashkins, *Chairman*.

WORCESTER (Worcester Section)

Friday, November 17, at 8:00 p.m., in the Staff Room of the Worcester City Hospital, Worcester. Pneumonia. Instructor: Maxwell Finland. George C. Tully, *Chairman*.

WORCESTER NORTH

Friday, November 17, at 4:30 p.m., in the Nurses' Home of the Burbank Hospital, Fitchburg. Medical Complications in Pregnancy. Instructor: James C. Janney. George P. Keaveny, *Chairman*.

CORRESPONDENCE

BLUE CROSS BENEFITS

To the Editor: Changes in benefits to Blue Cross subscribers were announced on September 1, 1939, and it is important that all members of the medical profession understand how they affect hospitalization of patients. These changes, approved by the board of directors of the Blue Cross and the State Commissioner of Insurance, were necessary to insure future stability and to protect the interests of all participants. The major changes are as follows: x-ray and anesthesia benefits are eliminated; maternity benefits are limited to half the hospital bill; and tonsil and adenoid operations are not included during the first year of membership. After the first year, the family representative is entitled to full benefits in these cases and his dependents to half benefits.

New certificates of membership will be issued to subscribers to become effective for each at the end of his current subscription year. In other words, a certain portion of the membership will be changed to the new certificate each month. Approximately 6000 subscribers were transferred to the new contract in September; another 13,000 will be changed in October, and so on, with those members enrolled during August, 1938, and August, 1939, remaining unchanged until August, 1940. Subscribers are entitled to all benefits under the old contract until they are transferred to the new certificate.

It is deplorable that benefits to the entire membership had to be limited chiefly because of abuses. Our experience has shown that abuses were practiced by subscribers and physicians alike, although they were, in the majority of cases, due to misunderstanding.

During two years of operation (to September 10, 1939), 225,000 subscribers were enrolled and total hospital bills paid in the amount of $1,225,000 for 25,000 patients, this sum representing about 85 per cent of the earned income for the period. With the Blue Cross's paying hospital bills for 25,000 patients, certainly hundreds of persons have been enabled to pay physicians' fees who otherwise would have received free care.

Specimen copies of the new certificate are available to physicians on request.

R. F. CAHALANE, *Executive Director*,
Associated Hospital Service Corporation.

21 Milk Street,
Boston.

NEW ENGLAND PEDIATRIC SOCIETY

To the Editor: The attention of the officers of the New England Pediatric Society has been called to the fact that it is believed generally that membership in the society is limited to pediatricians. This impression is entirely erroneous. The New England Pediatric Society is an organization devoted to the dissemination of a better understanding of the problems of infancy and childhood, and its membership includes many practitioners other than pediatricians. Its purpose can be accomplished only by enlarging the membership to include a greater number of physicians in New England who are interested in the care of infants and children. Any qualified physician who has such an interest is eligible for membership and will be welcomed into the society.

The society has previously held three or four meetings each year, usually in Boston, of clinical and scientific nature. It is planned that additional meetings be fostered in various parts of New England in order that those members unable to attend in Boston can keep informed of progress in this field of medicine. These would consist of round table discussions or clinical demonstrations rather than didactic lectures. Such meetings would necessarily be at the instigation of the local or county medical groups and would be under the direction of someone provided by the New England Pediatric Society.

Inquiries should be addressed to the secretary.

R. CANNON ELEY, *President*,
JAMES M. BATY, *Secretary*.

1101 Beacon Street,
Brookline, Massachusetts.

NOTICES

REMOVAL

FRED A. SIMMONS, M.D., announces the removal of his office to 264 Beacon Street, Boston.

ANNOUNCEMENT

KENDALL B. CROSSFIELD, M.D., announces the opening of an office at 99 Bay State Road, Boston.

BOSTON DISPENSARY

A luncheon meeting of the clinical staff of the Boston Dispensary will be held on Friday, November 24, in the auditorium of the Joseph H. Pratt Diagnostic Hospital at 12:00 noon. At 12:30 p.m., Dr. Henry A. Christian will speak on "Cardiocasualties."

An invitation is extended to all who are interested. The luncheon charge to non-members is 35c.

JAMES M. BATY, M.D., *Secretary*.

BOSTON LYING-IN HOSPITAL

Professor Bernhard Zondek will speak on "Ovulation and Menstruation" at the Boston Lying-in Hospital, on Friday evening, November 17, at 8:15.

Members of the medical profession are cordially invited to attend.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Dr. Burrill B. Crohn, chief of the Genitoinfectious Service and associate in medicine at Mt. Sinai Hospital, New York City, will speak on "Regional Ileitis" in the lecture hall of the Joseph H. Pratt Diagnostic Hospital, Saturday

morning, November 25, at 9:00. Physicians and medical students are cordially invited to attend.

SOUTH END MEDICAL CLUB

The next meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, November 21, at 12 o'clock noon. Dr. Oscar F. Cox, Jr., will speak on "Gonococcal Infection."

Physicians are cordially invited to attend.

JOHN B. HALL, M.D., *Secretary.*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Tuesday, November 14, in the amphitheater of the Peter Bent Brigham Hospital (Shattuck Street entrance), at 8:15 p.m. Dr. Soma Weiss will preside.

PROGRAM

Presentation of Cases.

Hemolytic Streptococcal Infections: Their importance in acute and chronic diseases. Dr. Chester S. Keefer.

Medical students and physicians are cordially invited to attend.

ROBERT M. ZOLLINGER, M.D., *Secretary.*

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will rehearse under Alexander Theide, former concert-master with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra, every Thursday at 8:30 p.m., in Studio A, Station WMEX, 70 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

CARNEY HOSPITAL

The monthly clinical meeting and luncheon of the Carney Hospital will be held in the Andrew Carney Assembly Room on Monday morning, November 20, at 11:30.

PROGRAM

Case Reports.

X-ray Visualization of the Biliary Tract. Dr. Herbert H. Finn. Discussion by Drs. A. McK. Fraser, A. J. Leary, L. F. Curran, J. J. Todd and W. C. Moloney.

Physicians and medical students are cordially invited to attend.

ROY J. HEFFERNAN, M.D., *Secretary.*

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, November 15, from 2 to 4 p.m. Drs. William C. Quinby and Soma Weiss will speak on "Dysuria." A clinicopathological conference, conducted by Dr. Elliott C. Cutler, will take place from 4 to 5 p.m.

On Thursday, November 16, from 8:30 to 9:30 a.m. there will be at the Peter Bent Brigham Hospital, a combined clinic, conducted by Dr. Elliott C. Cutler, of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital.

Physicians and students are cordially invited to attend.

ELLIOTT C. CUTLER, M.D., *Secretary.*

LAWRENCE CANCER CLINIC

The regular Lawrence Cancer Clinic, to be held at Lawrence General Hospital, 1 Garden Street, Lawrence, on Tuesday, November 21, at 10:00 a.m., will be a demonstration and teaching clinic for physicians, with Channing C. Simmons, M.D., of Boston, present as consultant. Physicians of the north half of Essex County are invited to accompany any of their patients whom they desire to have this service or to send them with a note. A report will be returned to every physician who sends a patient. The service is gratis. Any physician is welcome to attend the clinic.

This clinic is endorsed by the Committee on Postgraduate Instruction of the Massachusetts Medical Society.

ROY V. BAKETEL, M.D.,
CHARLES J. BURGESS, M.D.,
JOHN J. MCARDLE, M.D.,
HARRY H. NEVERS, M.D.,
THOMAS V. UNIAC, M.D.,
J. FORREST BURNHAM, M.D., *Chairman.*

NEW ENGLAND PATHOLOGICAL SOCIETY

The next meeting of the New England Pathological Society will be held on Thursday evening, November 16, at 8:00 at the Peter Bent Brigham Hospital.

Dr. Paul R. Cannon, professor of pathology at the University of Chicago, will speak on "The Relation of Flocculating Antibodies to Tissue Hypersensitiveness and Localized Disease."

Physicians and students are cordially invited to attend.

BENJAMIN CASTLEMAN, M.D., *Secretary.*

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

The annual meeting of the New England Obstetrical and Gynecological Society will be held in Boston on Wednesday, December 6.

The Carney Hospital, Massachusetts General Hospital and the Lahey Clinic will hold morning clinics, and an afternoon clinic is to be held at the Boston City Hospital.

INTERNATIONAL COLLEGE OF SURGEONS

The officers of the United States Chapter of the International College of Surgeons cordially invite all physicians and surgeons in good standing to their fourth assembly, to be held in Venice, Florida, February 11 – 14, 1940. There is no registration fee.

For general information please address Dr. Fred H. Albee, Chairman, 57 West 57th Street, New York City. For information about the presentation of scientific papers or exhibits, query Dr. Charles H. Arnold, Secretary of the Scientific Assembly, Terminal Building, Lincoln, Nebraska.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Monday, November 13

Monday, November 13

*12:15 p.m.–1:15 p.m. Clinicopathological conference. Dr. S. Burt Wolbach, Peter Bent Brigham Hospital amphitheater.

*12:30 p.m. Massachusetts Tuberculosis League. Y. W. C. A., Boston.

Tuesday, November 14

*9–10 a.m. "Cardiovascular Disorders in the Course of Some Acute Infectious Diseases." Dr. Conrad Wesselhoeft. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.

*12:15 p.m.–1:15 p.m. X-ray conference. Dr. Merrill C. Sosman. Peter Bent Brigham Hospital amphitheater.

*8:15 p.m. Harvard Medical Society. Amphitheater of the Peter Bent Brigham Hospital.

Wednesday, November 15

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital amphitheater.

*2 p.m.–4 p.m. Joint medical and surgical clinic. Peter Bent Brigham Hospital.

Thursday, November 16

*8:30 a.m.–9:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Peter Bent Brigham Hospital.

*9–10 a.m. "Recent Advances in Hematology." Dr. H. G. Brugsch. Joseph H. Pratt Diagnostic Hospital.

Friday, November 17

*9–10 a.m. "Peripheral Vasospasm in the Causalgia-Like States." Dr. John Homans. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.

12 m. Clinical meeting of the Children's Medical Service, Massachusetts General Hospital. Ether Dome.

*12 m. Urological conference at the Massachusetts General Hospital, lower amphitheater, Out-Patient Department.

*8:15 p.m. Boston Lying-in Hospital. Professor Bernhard Zondek will speak on "Ovulation and Menstruation."

Saturday, November 18

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12 m. Medical staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Soma Weiss.

*Open to the medical profession.

November 13 — Massachusetts Tuberculosis League. Page 718, issue of November 2.

November 14 — Harvard Medical Society. Page 759.

November 15 — Peter Bent Brigham Hospital. Joint medical and surgical clinic. Page 759.

November 16 — Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital. Page 759.

November 16 — New England Pathological Society. Page 759.

November 17 — Boston Lying-in Hospital. Page 758.

November 20 — Carney Hospital. Monthly clinical meeting and luncheon. Page 759.

November 21 — South End Medical Club. Page 759.

November 21 — Lawrence Cancer Clinic. Page 759.

November 24 — Boston Dispensary. Luncheon meeting of the clinical staff. Page 758.

November 25 — Joseph H. Pratt Diagnostic Hospital. Page 758.

December 2 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

December 6 — New England Obstetrical and Gynecological Society. Page 759.

December 8 — William Harvey Society. Page 676, issue of October 26.

December 14 — Pentucket Association of Physicians. 8:30 p.m., Hotel Bartlett, Haverhill.

January 6, June 8–11, 1940 — American Board of Obstetrics and Gynecology. Page 160, issue of July 27.

January 22–25, 1940 — American Academy of Orthopaedic Surgeons. Hotel Statler, Boston.

February 11–14 — International College of Surgeons. Page 759.

March 2, June 8 and 10 — American Board of Ophthalmology. Page 719, issue of November 2.

March 7–9, 1940 — The New England Hospital Association. Hotel Statler, Boston.

May 14, 1940 — Pharmacopoeial Convention. Page 894, issue of May 25.

June 7–9, 1940 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

District Medical Societies

ESSEX SOUTH

November 15 — "Heart Disease in Pregnancy." Dr. C. Sidney Burwell. Beverly Hospital, Beverly.

December 6 — "Pyelonephritis and Its Relation to Other Inflammatory Diseases of the Kidney." Dr. Soma Weiss. Salem Hospital, Salem.

January 3, 1940 — "Head Injuries." Dr. John S. Hodgson. Danvers State Hospital, Hathorne.

February 14 — "Cough, Sputum, Hemoptysis — How shall they be investigated?" Dr. Reeve H. Betts. Essex Sanatorium, Middleton.

March 6 — "Experimental and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcal Infections." Dr. Champ Lyons. Lynn Hospital, Lynn.

April 3 — Addison Gilbert Hospital, Gloucester.

May 8 — Annual meeting. Salem Country Club, Peabody.

HAMPSHIRE

January 10, 1940.

March 13.

May 8.

All meetings are held at 11:30 a.m. at the Cooley Dickinson Hospital, Northampton.

MIDDLESEX EAST

November 15.

January 10, 1940.

March 20.

May 15.

Meetings are held at 12:15 p.m. at the Unicorn Country Club, Stoneham.

PLYMOUTH

November 16 — Moore Hospital, Brockton.

January 18, 1940 — Brockton Hospital, Brockton.

March 21 — Goddard Hospital, Brockton.

April 18 — State Farm.

May 16 — Lakeville Sanatorium, Lakeville.

SUFFOLK

November 29 — Scientific meeting. Treatment of Syphilis. Dr. Harold T. Hyman, Dr. Louis Chargin, and Dr. William Leifer, of New York City.

January 31, 1940 — Scientific meeting. Subject to be announced later.

March 27 — Scientific meeting. Symposium on Ulcerative Colitis and Diarrheas. Under the direction of Dr. Chester M. Jones.

April 24 — Annual meeting in conjunction with the Boston Medical Library. Election of officers. Program and speakers to be announced later.

BOOKS RECEIVED FOR REVIEW

Atlas of Surgical Operations. Elliott C. Cutler and Robert Zollinger. 181 pp. New York: The Macmillan Co., 1939. $8.00.

A Topographic Atlas for X-Ray Therapy. Ira I. Kaplan and Sidney Rubenfeld. 120 pp. Chicago: The Year Book Publishers, Inc., 1939. $4.00.

An Introduction to Medical Mycology. George M. Lewis and Mary E. Hopper. 315 pp. Chicago: The Year Book Publishers, Inc., 1939. $5.50.

Problems in Prison Psychiatry. J. G. Wilson and M. J. Pescor. 275 pp. Caldwell, Idaho: The Caxton Printers, Ltd., 1939. $3.00.

You and Heredity. Amram Scheinfeld. Assisted by Morton D. Schweitzer. 434 pp. New York: Frederick A. Stokes Co., 1939. $3.00.

Gynecology: Medical and surgical. P. Brooke Bland. Assisted by Arthur First. Third edition. 843 pp. Philadelphia: F. A. Davis Co., 1939. $8.00.

Diagnostic Signs, Reflexes and Syndromes. W. Egbert Robertson and Harold F. Robertson. 309 pp. Philadelphia: F. A. Davis Co., 1939. $3.50.

A Text-Book of Occupational Diseases of the Skin. Louis Schwartz and Louis Tulipan. 799 pp. Philadelphia: Lea & Febiger, 1939. $10.00.

Physiology in Health and Disease. Carl J. Wiggers. Third edition. 1144 pp. Philadelphia: Lea & Febiger, 1939. $9.50.